Evaluation of Ethyl Parathion as a Toxic Air Contaminant

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This report has been reviewed and approved by the Scientific Review Panel established pursuant to Section 39670 of the Health and Safety Code.

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EXECUTIVE SUMMARY

The California Department of Food and Agriculture (CDFA) has prepared a report on ethyl parathion pursuant to Section 14023(a) of the Food and Agriculture Code.

Ethyl parathion was selected for evaluation as a toxic air contaminant for the following reasons. First, ethyl parathion is a widely used, broad spectrum insecticide-acaricide of high toxicity to mammals. Second, because of its relative volatility and because it is often applied by air or methods resulting in measurable atmospheric levels, it may be considered an air contaminant.

This report includes:

-a review of the available scientific evidence on ethyl parathion regarding its physical properties, environmental fate and human health effects,

-the results of measuring ambient airborne concentrations of ethyl parathion,

-an estimate of the levels of exposure in air which may cause or contribute to adverse health effects,

- and, an estimate of the range of risk to humans resulting from current or anticipated exposure to ethyl parathion in air.

The CDFA has determined that adverse health effects from ethyl parathion would be unlikely at the reported low air concentrations found in areas which are remote from the sites of application and handling. While the reported air concentrations of ethyl parathion at adjacent, off-site locations during and immediately following application were lower than values predicted to produce acute adverse health effects, accidental exposure at these sites, particularly in instances of misapplication, can present potential problems related to acute health effects.

The primary adverse health effect on which the margins of safety were based was cholinesterase inhibition. Other adverse effects which were observed in animal studies involving chronic exposure were neuropathy, retinopathy, and other ophthalmic effects. Certain subpopulations, such as infants, asthmatics, persons under medical treatment with β-blockers, and individuals being treated for neuromuscular disorders with anticholinesterase drugs, may be at an increased risk from exposure to ethyl parathion. Additionally, concurrent exposure to other anticholinesterase pesticides has not been addressed in this document and could be a factor in an overall assessment of risk related to cholinesterase inhibition.

A. Environmental Summary

In regard to use patterns, ethyl parathion is often repeatedly applied by fan or boom sprayers or by aircraft on a wide variety of orchard, row and field crops. There are two seasons of heavy use. During January and February, it is applied on orchards in the Central Valley. In September and October, it is used in the Imperial Valley on sugar beets.

After application, ethyl parathion may volatilize into the atmosphere or adsorb onto dust particles. In the environment, it follows two major pathways - degradation to less toxic compounds or oxidative conversion to the toxic bioactive product, paraoxon. The extent of conversion to paraoxon is dependent upon the amount of sunlight, atmospheric oxidants present, and the type of pesticide formulation applied. The persistence of ethyl parathion and paraoxon is associated with high clay dust levels and dry stable weather, whereas its disappearance is associated with rainfall.

Airborne levels of ethyl parathion have been extensively reported in the literature. The highest levels of parathion were reported in the wash down area for crop-dusting aircraft (320 $\mu g/m^3$) and in the cockpits of those aircraft during application (179 $\mu g/m^3$). These levels were followed by air levels of 48 and 43 $\mu g/m^3$ measured in the truck cab and tractor towing spray-rigs, respectively. Reported airborne levels of

ethyl parathion at the site of application ranged from 2 to 18 $\mu g/m^3$ within a day of application down to none detected to 0.005 $\mu g/m^3$ 21 days after application. Reported off-site downwind levels ranged from a high value of 34 $\mu g/m^3$ 40 yards from the sprayed field during application to 0.002 $\mu g/m^3$ 100 yards from the field 6 days later. Finally the range of reported ambient air levels of parathion was from 0.017 to 0.089 $\mu g/m^3$.

Ambient air levels of ethyl parathion and paraoxon were measured by the Air Resources Board (ARB) for the CDFA in the San Joaquin Valley from January 6, 1986 to February 14, 1986 and in the Imperial Valley from September 23 to October 22, 1986. In the ARB study, the highest individual 24-hour value measured was 1.423 $\mu g/m^3$ with a mean 24-hour value of 0.170 $\mu g/m^3$ for six sites in the northern San Joaquin Valley over the period of study of 23 days (Table 6). In the southern San Joaquin Valley and in the Imperial Valley, the amount of ethyl parathion in the air was considerably lower. The highest individual 24-hour value in the southern San Joaquin Valley was 0.089 $\mu g/m^3$ and in the Imperial Valley, 0.150 $\mu g/m^3$ (Table 6). Thus, despite the probability that large amounts of ethyl parathion were applied in the San Joaquin Valley during the period of time air samples were taken, airborne concentrations were low. The low values were probably the result of the wet, foggy weather prevailing during the winter months. In the Imperial Valley, the ambient levels of ethyl parathion were even lower. The amount of ethyl parathion used in the Imperial Valley was probably about one-sixth that used in the San Joaquin Valley (Table 4), and the increased volatility that might

have occurred because of the very warm weather of September and October did not seem to be sufficient to yield levels of airborne ethyl parathion above those found in the San Joaquin Valley.

B. Health Effects Summary

Parathion is an anticholinesterase, organophosphate insecticide. The cholinesterase inhibition is attributed to the oxygen analogue, paraoxon, which is produced both by environmental degradation and animal metabolism. Parathion is readily absorbed by all routes of administration and it is rapidly eliminated. While neither parathion nor its metabolites accumulate, residual suppression of cholinesterase (ChE) may last for weeks following exposure. Parathion is extremely toxic on an acute basis and the oral LD_{50} in the rat is between 3.5 mg/kg and 7.6 mg/kg.

The major health effect associated with parathion is inhibition of acetylcholinesterase (AChE), which has been observed following acute, subchronic and chronic exposures. A 30% or greater inhibition of acetylcholinesterase or plasma cholinesterase is considered to be a biologically significant depression and, therefore, 30% has been designated as the threshold for these effects. Other chronic health effects observed in the rat include retinopathy, neuropathy, and ophthalmic effects; however, these effects were only seen at dose levels where significant acetylcholinesterase inhibition was seen.

The oncogenic potential of parathion was assessed, and it was determined that there was only limited evidence of oncogenicity in animals. Therefore, a quantitative cancer risk assessment was not performed on this pesticide. This decision was based on the observations that a positive oncogenic response was observed in one strain of one species (Osborne-Mendel rat), the increased tumor incidence was in a tumor with a high background rate, and that two other studies were negative (one in Sprague Dawley rat and one in B6C3f1 mice). Additionally, definitive conclusions could not be made concerning the genotoxic potential of parathion.

A margin of safety (MOS) was determined for the NOEL (no observed effect level) for non-oncogenic effects. The MOS is the ratio of the NOEL over the exposure estimate. A MOS of 10 for cholinesterase inhibition is considered sufficient protection. Larger margins of safety are necessary for protection for other effects or if there are uncertainties in the data.

The lowest NOEL for the inhibition of RBC acetylcholinesterase from an acute exposure study is 1.21 mg/m^3 for a 4-hour exposure in the rat. This translates to an adult human equivalent air concentration of 4.48 mg/m^3 for the adult and 2.5 mg/m^3 for the child based on a 4-hour exposure. These values extrapolate to 0.75 mg/m^3 and a child equivalent of 0.42 mg/m^3 based on a 24-hour exposure. The MOS's for the highest exposure of 34 $\mu g/m^3$ (15-minute sample) are 100 and 74 for the adult and

child, based on a 4-hour NOEL. The MOS's for the highest 24-hour ambient air concentration of 1.423 $\mu g/m^3$ are 500 and 300 for the adult and child, respectively.

In studies using subchronic inhalation exposures (7 hr/day, 5 day/week, 6 weeks) the NOEL for cholinesterase inhibition was 0.01 mg/m^3 for both the rat and the dog. This converted to an adult human equivalent concentration of 0.011 mg/m^3 and a child equivalent of 0.006 mg/m^3 for the rat, and an adult equivalent of 0.004 mg/m^3 and child equivalent of 0.002 mg/m^3 for the dog. The MOS's for cholinesterase inhibition based on the rat data are 65 and 35 (adult and child) and the MOS's based on the dog data are 24 and 12 (adult and child) for a exposure concentration of 0.170 $\mu g/m^3$.

The NOEL for cholinesterase inhibition in a chronic feeding study in the dog was 0.01 mg/kg-day. The adult human equivalent is 0.039 mg/m^3 and the child equivalent is 0.02 mg/m^3. The MOS's of safety for cholinesterase inhibition are 200 and 100 (adult and child, respectively) with an exposure estimate of 0.170 $\mu g/m^3$. The lowest NOEL (2 ppm or 0.10 mg/m^3) from a chronic rat study was based on cholinesterase inhibition and ophthalmic effects. This provides MOS's of 2,200 (adult) and 1,200 (child) with the adult human equivalent concentration of 0.37 mg/m^3 and the child equivalent of 0.21 mg/m^3 using an exposure estimate of 0.170 $\mu g/m^3$.

The oral NOEL for RBC AChE inhibition in humans is 0.05 mg/kg/day (6 week exposure), which converts to an air concentration of 0.19 mg/m^3 for adults and 0.11 mg/m^3 for children. Using the mean exposure value of 0.170 $\mu g/m^3$, the MOS's for this effect are 1,000 and 600 for adults and children, respectively. The acceptable daily intake (ADI) for parathion of 0.005 mg/kg/day was established by FAO/WHO based on this NOEL. The highest mean exposure of 0.170 $\mu g/m^3$ is 1.5% of the ADI.

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EVALUATION OF ETHYL PARATHION AS A TOXIC AIR CONTAMINANT

I. INTRODUCTION

The signing into law of Assembly Bills 1807/3219 set forth a procedure for the identification and control of toxic air contaminants in California. Under this law, the California Department of Food and Agriculture (CDFA) is responsible for the regulation of toxic air contaminant (TAC) pesticides in their pesticidal use (Section 14021 et seq., Food and Agricultural Code). As part of the TAC identification process, the CDFA is required to prepare a report evaluating the health effects of candidate pesticides which may pose a present or potential hazard to human health due to airborne emissions from use.

This report on ethyl parathion contains 1) the physical and chemical characteristics, patterns of use and environmental fate of ethyl parathion as they may pertain to ethyl parathion's potential as an air contaminant; 2) the results of the study carried out by the Air Resources Board (ARB) at the request of the CDFA, which measured airborne levels of ethyl parathion; and 3) an extensive review of health effects, including:

-an estimate of the levels of exposure in air which may cause or contribute to adverse health effects,

-an assessment of the availability and quality of data on health effects, and

-where there is no threshold of significant adverse health effects, the range of risk to humans resulting from current or anticipated exposure to ethyl parathion present in air.

II. BACKGROUND

Ethyl parathion is an organophosphate insecticide-acaricide that has been in use since the late 1940's. Its fate follows two major pathways in the environment. It may be degraded by hydrolytic reactions to less toxic compounds, or it may be activated by oxidative conversion to paraoxon. The products resulting from environmental fate reactions are the same products resulting from the metabolism of parathion and are depicted in Figure 1. In the atmosphere, these fate reactions are usually accomplished through photolysis. The major phototransformation product is paraoxon (Woodrow et al., 1983). The effectiveness of ethyl parathion in insects and mammals is actually due to paraoxon which specifically inactivates acetylcholinesterase and results in the production of neurotoxic symptoms. Table 1 presents those physical and chemical characteristics of ethyl parathion and paraoxon which may affect the appearance of these two compounds in the atmosphere.

Despite its relatively high toxicity and the fact that some insects have developed resistance to ethyl parathion, it is still considered a useful pesticide and is popular, partly because it is inexpensive. Newer, more costly materials have replaced ethyl parathion where beneficial insects are present and selectivity is important.

Figure 1.

ENVIRONMENTAL FATE OF PARATHION

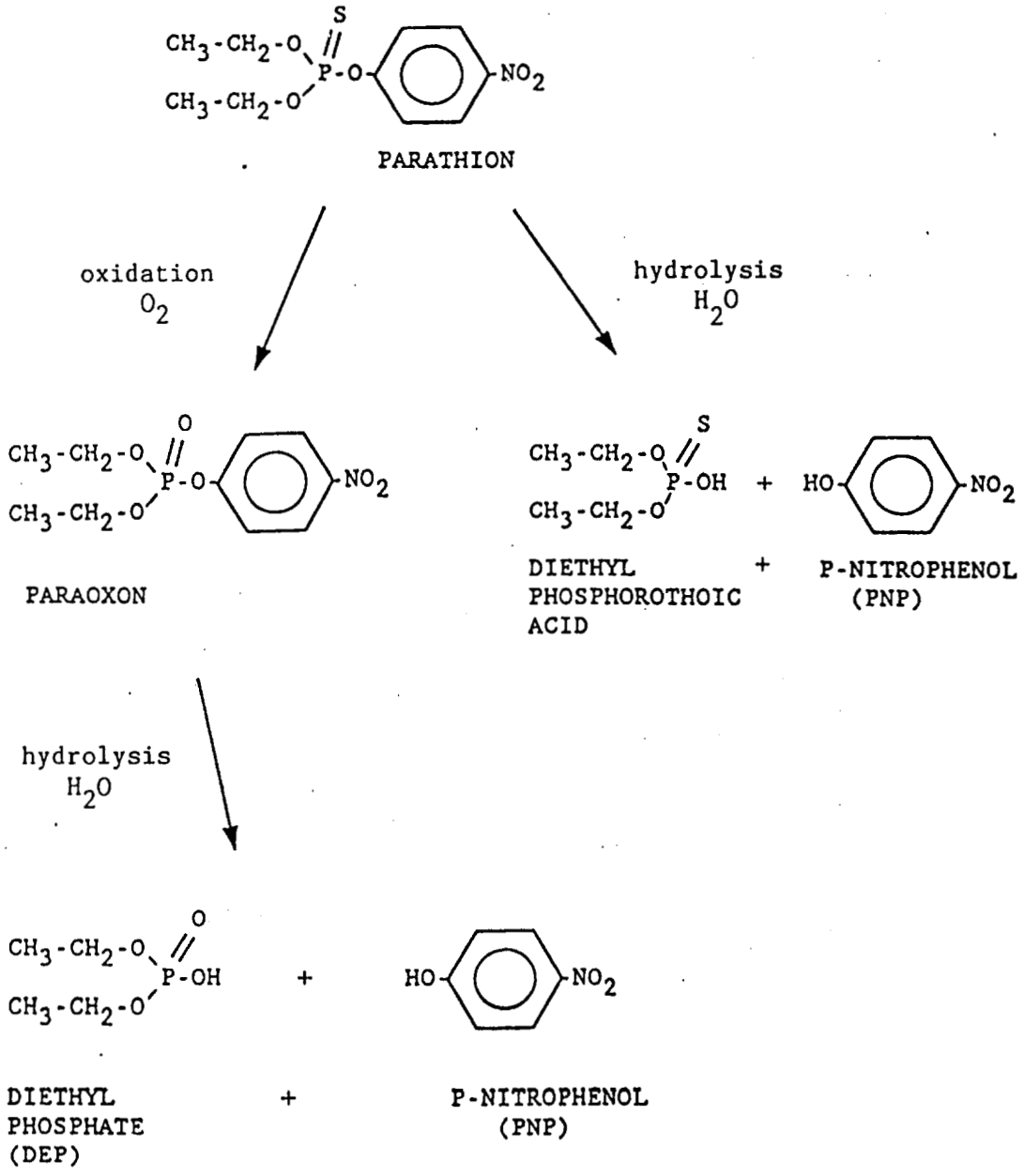

TABLE 1

CHARACTERISTICS OF ETHYL PARATHION AND PARAOXON

	Ethyl Parathion	Reference
Molecular Weight	291.3	Freed et al., 1979
Vapor Pressure	0.97×10^{-5} mm Hg (25°C)	Spencer et al., 1979
Volatility	0.09 mg/m^3	Melnikov, 1971
Water Solubility	24 µg/ml (25°C)	Williams, 1951
Boiling Point	113°C	Melnikov, 1971

	Paraoxon	
Molecular Weight	275.2	Spencer, 1968
Vapor Pressure	9×10^{-5} mm Hg (27.4°C)	Williams, 1951
Volatility	Not available	
Water Solubility	2400 µg/ml (25°C)	Williams, 1951
Boiling Point	169-170°C	Spencer, 1968

A. Toxicity and Regulation of Ethyl Parathion

Ethyl parathion is highly toxic to mammals (oral LD_{50} of 4 to 13 mg/kg in rats, Mulla et al., 1981) and has been implicated in a number of poisoning episodes of agricultural workers. Thus, reentry standards have been established by the CDFA. Workers may not reenter areas where applications have occurred for periods ranging from 2 to 90 days when application is approximately 0.5 to 8 pounds per acre, respectively (Title 3, California Administrative Code, Section 6772).

The CDFA prepares an annual summary of illnesses and injuries in California which are potentially related to pesticides. According to these summaries, 20 cases of systemic poisonings by parathion were reported in 1986, 16 in 1985, 18 in 1984 and 22 in 1983. These data represent a relatively high incidence of reported illnesses due to ethyl parathion over the most recent four years. Because of concern about such acute toxic effects as well as reports of acute avian toxicity, parathion has been placed into an accelerated special review process at the U.S. Environmental Protection Agency (EPA). The results of this review are expected by July 1988 (personal communication).

Since ethyl parathion is a category one (highly toxic) restricted material (Title 40, Code of Federal Regulations, Section 162.10), it may only be used under permit and use conditions administered by the County

Agricultural Commissioner. Regulatory procedures require users to file a pesticide use report within the county of use when this material is applied. Information contained in the annual Pesticide Use Report published by the CDFA is based on these individual reports to the counties. Table 2 summarizes use report data for 1983, 1984, and 1985 by commodity. Table 3 identifies the counties where ethyl parathion was most heavily used and the time of year when it was most often applied in 1985. Table 4 presents the counties which used the most ethyl parathion in 1985 and the rural population of each of these counties from the 1980 census.

B. Application

1. Timing of Application

There are two seasons when ethyl parathion is most frequently applied. In 1985, according to the Pesticide Use Report, it was applied heavily in January and February on crops in the Central Valley counties of Kern, Fresno, and Tulare. Smaller amounts were used in September and October in Imperial county (Table 3). During 1985, Kern County used the most ethyl parathion (107,000 pounds of active ingredient, 15% of total used in California), while Imperial County used approximately half that amount (53,000 pounds of active ingredient, 7% of total, Table 4).

TABLE 2

ETHYL PARATHION USE BY COMMODITY

(in thousands of lbs active ingredient)

	1983		1984		1985	
Commodity	Lbs	%	Lbs	%	Lbs	%
Orchard	371	56	479	64	480	64
Citrus	77	12	62	8	40	5
Grape	46	7	15	2	19	3
Broc/Lett	26	4	27	4	33	4
Field Crops	40	6	38	5	76	10
Sugar Beets	23	4	34	5	30	4
Tomatoes	16	2	15	2	10	1
Other	64	9	74	10	69	9
Total	663	100	744	100	758	100

TABLE 3
MONTHLY ETHYL PARATHION USE IN 1985 BY COUNTY
(in thousands of lbs active ingredient)

January		February		March		April		May		June	
County	Lbs	County	Lbs	County	Lbs	County	Lbs	County	Lbs	County	Lbs
Kern	51	Fresno	18	Fresno	9.1	Tulare	11	San Joaq	9.9	Tulare	9.7
Fresno	42	Kern	15	Tulare	6.6	Fresno	5.5	Tulare	9.6	Kern	2.5
Tulare	29	Tulare	13	Riversid	2.3	Kern	4.2	Stanisla	7.5	Monterey	2.1
Merced	28	Sutter	7.7	Kern	1.5	San Joaq	4.0	Merced	6.1	Fresno	1.6
Stanisla	25	Madera	4.3			Monterey	2.5	Fresno	5.1	Madera	1.4
Butte	22	Yuba	4.3			Riversid	1.4	Monterey	3.8		
Sutter	20	Glenn	3.6					Kern	1.7		
Madera	17	Butte	2.5					Sutter	1.5		
Yuba	13	Monterey	1.5								
San Joaq	13										

July		August		September		October		November		December	
County	Lbs	County	Lbs	County	Lbs	County	Lbs	County	Lbs	County	Lbs
Tulare	5.1	Monterey	3.7	Imperial	23	Imperial	19	Monterey	1.7	Kern	28
Fresno	4.4	Imperial	2.2	Riversid	6.6	Riversid	2.9	Imperial	1.7	Stanisla	12
San Joaq	3.8	Butte	2.0	Monterey	4.0	Monterey	2.4			Merced	10
Modoc	2.7	Fresno	1.8	Fresno	2.1	Tulare	1.2			Sutter	7.6
Siskiyou	2.0	Tulare	1.2	Yuba	1.3					Fresno	6.8
Butte	1.4									Tulare	6.4
Imperial	1.4									Butte	3.5
Los Ange	1.4									Madera	3.0
										Glenn	1.7
										San Joaq	1.6

Revised 3 February 88

TABLE 4
COUNTIES USING THE MOST ETHYL PARATHION IN 1985
AND THEIR TOTAL RURAL POPULATIONS

County	Lbs[a]	% Total Applied	Total Rural Population[b]
Kern	107	15	72,591
Fresno	98	14	111,520
Tulare	95	13	92,519
Imperial	53	7	27,860
Merced	50	7	50,772
Stanisla	48	7	50,695
Sutter	38	5	17,229
San Joaq	37	5	61,363
Butte	34	5	41,922
Madera	27	4	32,990

a In thousands of pounds active ingredient
b 1980 U.S. Census

Revised 9 May 88

2. Methods

Ethyl parathion is an active ingredient, e.g., the biologically active chemical in a pesticide formulation, in 40 currently registered pesticide products (as of May 1988). Wettable powder formulations and emulsifiable concentrates are preferred for use on dormant orchards and on field and orchard crops, respectively. It is used on a wide variety of orchard, row and field crops, many of which may receive multiple applications on an as-needed basis for the control of a broad spectrum of fruit, nut, vegetable, field and forage insects.

Ethyl parathion is usually mixed with water and applied by orchard fan sprayers, boom sprayers or aircraft at a rate of less than one to 6 pounds of active ingredient per acre. Even under special circumstances, no more than 8 pounds per acre may be applied to any crop. Twenty-eight percent of all applications in California are estimated to be by aircraft (Pesticide Use Report, 1984).

C. Environmental Fate

After application, the atmospheric presence of ethyl parathion may result from volatilization into the atmosphere or adsorption onto dust particles which may be suspended in air. Two factors contributing to the extent of volatilization or dissipation of ethyl parathion include air

temperature and product formulation. The vapor pressure of ethyl parathion increases with increasing temperature, therefore, ethyl parathion is likely to volatilize from surfaces more quickly and thus be released into the atmosphere more readily at higher temperatures (Spencer et al., 1979). Dissipation is also affected by the type of formulation used, with emulsifiable concentrates dissipating more rapidly than wettable powders (Gunther et al. 1977).

Chemical processes which may act upon atmospheric ethyl parathion include photolysis and reactions with ozone and OH and NO_3 radicals.

1. Conversion to paraoxon

Biologically, the most important chemical reaction of ethyl parathion in the environment is its conversion to paraoxon. In one study, ethyl parathion in the vapor phase was not affected by simulated sunlight, whereas parathion residues adsorbed onto particles were rapidly converted to paraoxon (Moilanen et al., 1975). However, more recent laboratory and field studies suggest that the conversion of ethyl parathion to paraoxon occurs largely in the vapor phase with a conversion half-life ($t_{1/2}$) ranging from 1 to 10 minutes during the day (Woodrow et al., 1977). The conversion $t_{1/2}$ is 2 minutes in midday summer sunlight (Woodrow et al., 1978). Since the $t_{1/2}$ lengthens to 131 minutes after sunset, the conversion seems to be dependent primarily on sunlight and atmospheric pollutants present during daylight hours (Woodrow et al., 1978).

Early studies suggested even more rapid conversion in the presence of high ozone levels (Woodrow et al., 1978; Spear et al., 1978; Spencer et al., 1980b). However, ozone may not be of primary importance in the formation of paraoxon (Woodrow et al., 1983). Goodman et al. (1988) recently reported the results of gas-phase reactions of trimethyl phosphorothioates with the atmospheric contaminants, OH and NO_3 radicals and ozone. Trimethyl phosphorothioates are structurally similar to parathion. These investigators found that the trimethyl phosphorothioates do not react with either ozone or the NO_3 radical. Instead, the dominant chemical reaction of these organophosphorus compounds is oxidation by the hydroxyl radical (Atkinson et al., 1988). With a rate constant of 9×10^{-11} cm^3 $molecule^{-1}$ s^{-1}, in the presence of 1×10^6 OH radicals/cc, R. Atkinson estimated that parathion may be expected to have a lifetime of approximately 3 hours in daylight (personal communication). The rate constant for the reaction of OH radicals with paraoxon is about three times slower than for parathion, and thus paraoxon would be expected to have a longer lifetime in the atmosphere.

Formulation type affects the extent of conversion; application of wettable powder results in higher paraoxon levels compared to the application of the same amount of emulsifiable concentrates (Winterlin et al., 1975; Gunther et al., 1977). The simultaneous addition of the agricultural nutrient, zinc oxide, increases the oxidation to paraoxon (Popendorf and Leffingwell, 1978).

Subsequent hydrolytic breakdown of ethyl parathion and paraoxon to the environmentally stable compound, p-nitrophenol, can become significant 14 to 21 days after application (Woodrow et al, 1977), indicating a relative resistance to hydrolysis compared to oxidation. Consistent with this observation, the hydrolysis rate (half-life) of ethyl parathion was found to be 26.8 days in the laboratory (Freed et al., 1979).

2. Persistence

The persistence of paraoxon in the environment seems to be dependent upon the nature and level of dust present, with increased persistence related to high clay content (Adams et al, 1977; Spencer et al., 1980a) and increased dust levels (Spear et al, 1978; Spencer et al., 1980a,b; Winterlin et al., 1982)). The effect of dust on paraoxon persistence was studied by Spencer et al. (1980b). These investigators found that, when applied to glass, the majority of the pesticide dissipated (80% of the amount applied), whereas, application to San Joaquin Valley soil dust resulted in the majority of the pesticide remaining in the dust (75% of the amount applied). This increased persistence is reflected in the $t_{1/2}$ of the dissipation of paraoxon from dust particles which has been found to be greater than 22 days (Adams et al., 1977). Under certain conditions, the $t_{1/2}$ of paraoxon or its parent, parathion, may be even longer. At high application rates and with repeated applications, parathion has been found up to 16 years later (Mulla et al, 1981).

3. Effect of Weather

Dry stable weather, dusty conditions and a high level of ozone are conducive to the production and persistence of paraoxon. These conditions generally describe the environment of California's Central and Imperial Valleys during the summer months (Spear et al., 1978). Conversely, rainfall is highly correlated with paraoxon disappearance (Nigg et al., 1979b), suggesting that wet weather would lead to greatly reduced levels of atmospheric parathion and paraoxon. These weather-related factors are most likely responsible for the high number of reported parathion poisonings of field workers in the Central Valley compared to the few episodes reported in Florida where dry spells are rare (Spear et al., 1975; Spear et al, 1978). Other climatic conditions, such as the speed and direction of the wind, contribute to the appearance and persistence of ethyl parathion in the environment. For example, this pesticide has been found in air samples taken from areas where no application of ethyl parathion was ever made (Carman et al., 1952).

D. Airborne levels Reported in the Literature

1. Occupational Exposures during Application

In Israel, Cohen et al. (1979) measured air levels of parathion at the airport where pesticides were loaded. Measurements ranged from 4 to 63

$\mu g/m^3$ (mean 24.6 $\mu g/m^3$, n=9) at the air strip, 12 and 97 $\mu g/m^3$ (n=2) in the hanger, and 290 and 350 $\mu g/m^3$ (n=2) in the aircraft washing area (Table 5A). These same investigators measured air levels of ethyl parathion in the cockpits of crop-dusting planes during application and found 0 to 430 $\mu g/m^3$ (mean 179 $\mu g/m^3$, n=12) for sampling periods of less than 21 minutes (Table 5A).

Carman et al. (1982) measured air levels to which a driver of ground spray rigs applying parathion would be exposed. Ethyl parathion was applied to citrus trees in California with a spray rig towed by either a tractor or truck with both windows open. Samples were collected during application. Tractor drivers were exposed to parathion air levels ranging from 12 to 68 $\mu g/m^3$ (mean 43.4 $\mu g/m^3$, n=9). In a truck cab, the air levels ranged from 3 to 93 $\mu g/m^3$ (mean 48.0 $\mu g/m^3$, n=5)

2. Airborne Levels at Site of Application

Measurements of airborne levels of ethyl parathion and paraoxon during and following applications to specific sites were done by several investigators and are summarized in Tables 5B and 5C. Table 5B depicts measurements taken within the field being sprayed. Mean airborne levels of ethyl parathion were reported to be 50 $\mu g/m^3$, 30 $\mu g/m^3$, and 90 $\mu g/m^3$ in orchards sprayed by aircraft, air-blast sprayer, and high-pressure hand sprayer, respectively (Batchelor and Walker, 1954).

TABLE 5A
AIRBORNE LEVELS OF ETHYL PARATHION
REPORTED IN THE LITERATURE

AIRBORNE LEVELS RELATED TO OCCUPATIONAL EXPOSURE

Location	Mean of Positive Samples $\mu g/m^3$	Maximum Value $\mu g/m^3$	Comments	Reference
Air strip loading area	24.6	63		1
Hanger	54.5	97		
Aircraft washing area	320	350		
Cockpit	179	430	11-21 min.[a]	
Cockpit	50	410	35-260 min.[a]	
Truck cab	48	93		2
Tractor	43.4	68		

[1] Cohen et al. 1979

[2] Carman et al. 1982

[a]Sampling period.

TABLE 5B
AIRBORNE LEVELS OF ETHYL PARATHION AND PARAOXON
REPORTED IN THE LITERATURE

AIRBORNE LEVELS AT SITE OF APPLICATION

Time after Application hours (days)	Parathion µg/m³	Paraoxon µg/m³	Comments	Reference
0	50		During aircraft application	1
0	30		During sprayer application	
0	90		During hand sprayer applica.	
2-4	18.2	0.2	Vapor concentration	2
72 (3)	4.7	0.3		
240 (10)	1.8	<0.1		
0-2	1.7		15 minute samples	3
4	3.3			
8	2.5			
12	1.0			
24	None detected			
48	None detected			
Days				
1	5.0		4 hour samples	4
3	2.5			
6	0.5			
8	0.1			
0	3.554	0.302	1974 study	5
1	0.442	0.154		
2	0.103	0.054		
3	0.053	0.026		
5	0.023	0.014		
14	0.006	0.003		
21	0.005	0.002		
0	-	-	1975 study	
1	4.100	0.611		
2	0.394	0.128		
3	0.397	0.127		
5	0.149	0.070		
14	0.021	0.015		
21	0.016	0.006		

[1]
[2]Batchelor and Walker, 1954
[3]Gunther et al. 1977
[4]Maddy et al. 1982
[5]Nigg et al. 1979
Woodrow et al. 1977

Gunther et al. (1977) measured both parathion and paraoxon vapors in citrus groves after treatment with 10 lbs/acre. The parathion and paraoxon values are the mean of positive samples only taken at specific days after various applications. Paraoxon was detected in 5 of 19 samples at levels of <0.1 to 0.3 $\mu g/m^3$.

In a peach orchard in Tulare County, 2.5 lbs/acre of ethyl parathion was applied. Maddy et al. (1982) began their measurements of airborne levels of ethyl parathion as soon as the spray had dried. 2.5 lbs/acre was applied. Mean values of 3 or 4 samples at each time interval are shown. No background levels were reported.

In the study carried out by Nigg et al. (1977), ethyl parathion at a rate of 4 lbs/acre was applied to a citrus grove in Florida. No paraoxon was detected, and the background level of ethyl parathion was less than 1 $\mu g/m^3$. The values represent the mean of two experiments, one carried out in July and the other carried out from October through November.

Woodrow et al. (1977) applied 2 lbs/acre of ethyl parathion to a plum orchard in Parlier (Fresno County) in August 1974 and again in July 1975. The pre-application background level was 0.001 $\mu g/m^3$ for both ethyl parathion and paraoxon. Two to 4-hour samples were taken on each of the indicated days. In the 1974 study, on-site measurements were initiated approximately 1 hour after application. In 1975, samples within the orchard were taken beginning on the day following application.

3. Airborne Levels off-site Downwind from Application

In Table 5C the results of two studies which measured airborne levels of ethyl parathion downwind near the field being sprayed are shown. In the first study, Maddy et al. (1983) measured airborne levels during and just after application of 2.5 lbs/acre of ethyl parathion to an orchard in Los Angeles County in the spring. During application 15 to 20-minute samples were taken between 40 and 75 yards from the edge of the orchard. The second study (Woodrow et al. 1977) was part of the July 1975 application of 2 lbs/acre described above. Samplers were set up 109 and 438 yards downwind from the plum orchard in Parlier, and 2 to 4-hour samples were taken.

The reported airborne levels of ethyl parathion range from 1.7 to 90 $\mu g/m^3$ in the field during or immediately following application. These levels fall rapidly with time to levels ranging from none detected to 5.0 $\mu g/m^3$ 24 hours after application. Approximately 40-50 yards downwind from fields being sprayed, 9.2 to 33.9 $\mu g/m^3$ of ethyl parathion were measured during application. Within 2 hours air levels fall approximately 10-fold. One hundred-nine yards and 438 yards downwind, airborne levels of 1.621 $\mu g/m^3$ and 0.123 $\mu g/m^3$, respectively, were measured immediately after spraying. These data suggest that the increased distance of 300 yards from the sprayed field could result in a 10-fold decrease in the airborne concentration of ethyl parathion.

TABLE 5C
AIRBORNE LEVELS OF ETHYL PARATHION AND PARAOXON
REPORTED IN THE LITERATURE

AIRBORNE LEVELS OFF-SITE DOWNWIND FROM APPLICATION

Distance from site (Yards)	Time after Application (Hours)	Parathion $\mu g/m^3$	Paraoxon $\mu g/m^3$	Reference
40	During appl.	24.8	a	Maddy et al. 1983
40	During appl.	33.9		
40	0-2	2.26		
40	0-2	3.09		
50	During appl.	9.2		
50	0-2	1.66		
20	0-2	3.57		
75	0-2	1.19		
109	0-1	1.621	0.403	Woodrow et al. 1977
109	5	0.756	0.051	
109	48	0.035	0.029	
109	72	0.009	0.009	
109	144	0.002	0.002	
438	0-1	0.123	0.060	
438	5	0.272	0.036	

a Samples were not analyzed for paraoxon.

4. Ambient Airborne Levels

Measurments of ambient airborne levels of ethyl parathion have been made by several investigators and are summarized in Table 5D. Stanley et al. (1971) performed a study of ambient air levels of ethyl parathion at 9 urban and rural sites in the United States, including urban locations in Fresno and Riverside in California. Monitoring took place over a 6-month period which included periods when applications would be expected and when pesticide usage would be at a minimum. No airborne parathion was detected at either California site. Ethyl parathion was only found in samples taken in Florida, and the values shown in Table 5D were selected by these investigators to illustrate the degree of variation found rather than the frequency of detection.

The study carried out by Kutz et al. (1976) was quite extensive with ambient air being collected at selected sites in 14 states in 1970 and 16 states in 1971 and 1972. The sampling locations included both rural and urban sites, chosen for their potentially high concentration of pesticides in ambient air. California was not included in this study. Three percent of samples collected in 1971 (25 of 787) and 2 percent (15 of 667) of samples collected in 1972 were positive for ethyl parathion. In 1972 none of the 1025 ambient air samples collected contained ethyl parathion.

TABLE 5D
AIRBORNE LEVELS OF ETHYL PARATHION
REPORTED IN THE LITERATURE

AMBIENT AIRBORNE LEVELS

Location	Total Number of Samples	Total Number of Positive Samples	Maximum Value $\mu g/m^3$	Mean of Positive Samples $\mu g/m^3$	
Florida	14	7	0.025	0.017	Stanley et al. 1971
Florida	14	14	0.465	0.089	
Various					Kutz et al. 1976
1970	787	25	0.834	0.064	14 states
1971	667	15	0.109	0.009	16 states
1972	1025	None	-	-	16 states
California					CDFA, 1988
1	10	10	0.077	0.041	Sites in
2	10	7	0.089	0.030	Imperial
3	10	9	0.188	0.055	Valley
4	11	11	0.031	0.018	
5	10	10	0.106	0.028	
6	7	7	0.214	0.070	
7	10	10	0.054	0.023	
8	10	10	0.103	0.047	

The CDFA performed an air monitoring study in the Imperial Valley during the first 2 weeks in October, 1986 (unpublished data). This study was carried out within the same time frame as the study performed by the ARB and described in Section III (Study 2). Monitoring was done at 8 rural sites. The means of samples positive for ethyl parathion ranged from 0.018 to 0.070 $\mu g/m^3$ at each site, while the overall mean for all sites was 0.040 $\mu g/m^3$. The highest single value measured was 0.213 $\mu g/m^3$. Ninety-five percent of all samples taken were positive for ethyl parathion.

Although not shown in Table 5D, Carman et al. (1952) monitored air levels of parathion in various areas of California and reported a mean of 187 $\mu g/m^3$ and a maximum value of 330 $\mu g/m^3$. These values are the highest ambient levels that have been reported in the literature. The results may be due to the method of analyses, since background levels measured by these investigators were also very high. For example, at sites where no parathion residues would be expected, airborne levels ranged from 70 $\mu g/m^3$ at the ocean to 170 $\mu g/m^3$ over an orange grove that had never been treated.

Table 5D shows that, although ambient atmospheric levels of parathion and paraoxon as vapor and adsorbed onto particulate matter have been reported and can be persistent, their levels are very low.

5. Ambient Airborne Levels in Fog

As seen in Table 3, ethyl parathion use is very high in January and February in the San Joaquin Valley. Heavy fog is a common occurence in the valley during that time period. Glotfelty et al. (1987) monitored for airborne parathion in heavy fog in rural areas including 3 locations in the central valley of California. The results of this study suggested that vegetation saturated with fog liquid may be a major source of exposure to pesticides and that fog may provide a vehicle for atmospheric transport of such pesticides over some distance. These investigators found that levels of parathion in the vapor phase ranged from 0.0009 to 0.008 $\mu g/m^3$, whereas fog water contained between 5.8 to 51.4 $\mu g/l$. Further work demonstrated that the liquid water content of fog air ranged from 0.02 to 0.07 g/m^3 (personal communication). Using this information total airborne parathion levels (e.g., the parathion level in the amount of fog water present in a cubic meter plus the parathion present as vapor) may be calculated. These calculated values range from 0.0013 to 0.0115 $\mu g/m^3$ which are at the low end of those ambient air values shown in Table 5D.

Levels of airborne paraoxon were also measured, and, again correcting for the amount of fog water in a cubic meter, the calculated values for the total paraoxon present in vapor and in fog liquid range from 0.0001 to 0.0131 $\mu g/m^3$. These levels are comparable to those found for parathion.

The source of paraoxon may be atmospheric conversion of parathion or conversion on surfaces followed by volatilization and subsequent scavenging by fog droplets. Conversion within fog droplets via the reaction with some unknown oxidant in the droplet is not considered likely (personal communication).

E. Use of Models to Estimate Air Levels of Ethyl Parathion

At present, there are no available models specifically designed to simulate pesticide dispersion after application. However, the ARB did use the Industrial Source Complex Dispersion Short-Term (ISCST) air quality model developed by the Environmental Protection Agency to determine locations in the San Joaquin Valley which could be expected to have high ambient air concentrations of ethyl parathion (Memorandum from D. McNerny, ARB, to W.V. Loscutoff, ARB, July 31, 1985, Recommendations for Parathion Monitoring Locations). Input data came from the Pesticide Use Reports published by the CDFA, from historical meteorological information, and from emission rate estimates from monitoring studies of parathion carried out by Woodrow et al. (1977). The information obtained was used to choose sampler sites for Study 1 described in Section III.

The results of this modeling study suggested that Reedley, followed by Parlier and Sanger, would be areas of high ambient air ethyl parathion concentration in January. The model proposed Wasco and McFarland as

areas with high air parathion levels in February. The results of the monitoring study performed by the ARB (Study 1, Section III) showed that Parlier, Reedley and Dinuba had the highest measured ambient air concentrations of ethyl parathion during January (1.423, 0.761, and 0.375 $\mu g/m^3$, respectively, Tables 6-8) as well as the highest percentages of positive samples. During February, McFarland and Wasco had the highest measured air levels of ethyl parathion and the highest percentages of positive samples (0.089 and 0.069 $\mu g/m^3$, respectively, Tables 6-8).

The ISC model has numerous features which may be utilized to estimate pesticide concentrations in air including: the capability of simulating area sources, the ability to consider gaseous and aerosol transport, the ability to consider rural areas, and the ability to provide concentration estimates for 1-hour to annual averages (EPA-450/4-86-005a). It has been validated and used for regulatory purposes by several government agencies, although it has not been specifically validated for pesticide releases. Among its disadvantages as a model for use in pesticide dispersion estimation is that it is a steady state model designed to provide peak concentration values near emission sources. It is not well suited for estimations at distances greater than 20 or 30 kilometers. It does not include mechanisms to account for chemical conversions. Further, the quality of many important inputs is quite poor or even non-existent. Among the input data that are lacking in quality are: vaporization rates (emission rates) of specific pesticides from leaf, soil and water after application, data regarding flux between aerosol and

vapor phases, the effect of cropping patterns on volatilization, and wind and other meteorological data representative of specific agricultural areas.

There are several other air models which have the potential to estimate pesticide dispersion but which have not been used or validated for that purpose. These include PAL which is similar to the ISC model (Peterson and Rumsey, 1986) and INPUFF which differs from the ISC and PAL models in that it may be used for the estimation of acute short-term, non-steady state air levels (Petersen and Lavdas, 1986).

F. Exposure

Human exposure to ethyl parathion or its toxic analog, paraoxon, can occur by three routes. Inhalation of vapor resulting from the dissipation of the pesticide from foliage to the atmosphere may occur. Exposure may be by inhalation of respirable dust particles (< 7 um) laden with parathion or paraoxon or by ingestion of those larger particles trapped by mucous and then swallowed. For occupational exposure, these two routes are minor compared to dermal absorption, as several studies have demonstrated that the highest intake results from absorption of this pesticide present on foliage or in dust through the skin (Batchelor and Walker, 1954; Ware and Morgan, 1976; Nigg et al., 1979b). Both dermal and respiratory exposure are greater when a wettable powder formulation is used than when an emulsifiable concentrate is used (Wolfe et al.,

1975). For ambient exposure, inhalation of vapors or dust particles followed by nearly total absorption through the pulmonary alveoli may be the primary route.

Airborne concentrations of ethyl parathion are dependent on both the intrinsic properties of ethyl parathion and environmental factors. However, the importance of atmospheric parathion and/or paraoxon, in regard to their possible adverse health effects, may lie more in their synergistic or additive interaction with other airborne pesticides/contaminants or the occasional circumstance when a combination of factors leads to increased persistence of parathion and/or paraoxon over time with the attendant possibility of subchronic exposure.

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PR - Peer reviewed
NPR - Non peer reviewed
UNK - Unknown
* - Cited in Parts II, III

- Date of literature search: March 1988.
- This bibliography emphasizes the atmospheric fate of and sampling and analytical techniques for ethyl parathion. It includes all references pertinent to these areas that were received in response to the information request sent out by the CDFA on 1 March 1985.

III. DOCUMENTATION OF AMBIENT AIRBORNE LEVELS

(Ambient Air Monitoring of Ethyl Parathion)

Summary

The ARB measured airborne levels of ethyl parathion in the San Joaquin Valley during the winter and in the Imperial Valley during the late summer coinciding with historically known times of peak application. Ethyl parathion levels measured in the San Joaquin Valley were higher than those measured in the Imperial Valley. Mean 24-hour values for the study period at each site in the San Joaquin Valley ranged from below the minimum detection level (MDL, 0.01 $\mu g/m^3$ or 0.8 ppt) to 0.232 $\mu g/m^3$ (18.9 ppt) with a maximum single 24-hour value of 1.423 $\mu g/m^3$ or 117.50 ppt. The overall mean of all samples positive for ethyl parathion collected at all sites during the study period was 0.170 $\mu g/m^3$ (14.09 ppt) for the northern San Joaquin Valley and 0.037 $\mu g/m^3$ (3.03 ppt) for the southern San Joaquin Valley. Those samples collected in the Imperial Valley ranged from 0.017 $\mu g/m^3$ (1.4 ppt) to 0.044 $\mu g/m^3$ (3.6 ppt) with a maximum single 24-hour value of 0.150 $\mu g/m^3$ (12.0 ppt). The overall mean of all samples positive for ethyl parathion collected at all Imperial Valley sites during the period of study was 0.028 $\mu g/m^3$(2.25 ppt). Paraoxon, the active degradation product of ethyl parathion, was detected in 6 of 133 individual samples collected in the San Joaquin Valley and was not detected in samples collected in the Imperial Valley (MDL: 0.02 $\mu g/m^3$ or 1.6 ppt). Paraoxon was detected only in samples collected in the

northern San Joaquin Valley. Paraoxon levels were converted to ethyl parathion equivalent values, weighted for its increased toxicity and added to the parathion values for those samples. Data are summarized in Tables 6 and 7. These tables present the highest and second highest 24-hour values observed at each location as well as the means and medians of the 24-hour samples positive for ethyl parathion only (number of samples above the MDL).

A. Introduction

On February 13, 1985, the CDFA requested that the ARB monitor ambient airborne levels of ethyl parathion. A monitoring recommendation, including information regarding ethyl parathion's chemical and physical characteristics and patterns of use, was sent to the ARB on December 5, 1985.

The CDFA recommended that the ARB monitor ambient levels of ethyl parathion in January or February in Fresno, Tulare and Kings Counties of the San Joaquin Valley because of the heavy use of ethyl parathion in those counties on deciduous orchards during the winter, and in September or October in Imperial County because of its use on row crops, such as sugar beets, during that time. Although the amount of ethyl parathion used in the Imperial Valley is less than that used in the San Joaquin Valley, it was believed that the greater volatility of ethyl parathion at higher temperatures might lead to increased atmospheric levels in the

TABLE 6 SUMMARY OF AMBIENT AIR CONCENTRATIONS OF ETHYL PARATHION AND ETHYL PARAOXON CONVERTED TO ETHYL PARATHION IN 24-HOUR SAMPLES in $\mu g/m^3$

	Location	Highest Value	Second Highest Value	# Above MDL	Mean[a]	±SD	Overall Mean[a]	Median[a]	Total # of Samples
STUDY 1	Sanger	0.193	0.100	7	0.073	0.062	**0.170**	0.078	11
	Parlier-1	**1.423**	1.204	12	0.314	0.473		0.118	13
Northern	Parlier-2	0.164	0.157	10	0.093	0.055		0.088	10
San Joaquin	Reedley	0.761	0.508	13	0.257	0.220		0.186	13
Valley	Dinuba	0.375	0.289	13	0.130	0.120		0.073	13
	Selma	0.277	0.260	8	0.152	0.084		0.143	13
	Earlimart	0.060	0.051	2	0.056	0.006	0.037	0.056	6
	Delano-1	0.015	0.016	2	0.016	0.001		0.016	7
Southern	Delano-2	<0.010	<0.010	0	<0.010	0		<0.010	5
San Joaquin	McFarland	0.089	0.073	5	0.042	0.037		0.025	7
Valley	Wasco	0.069	0.024	4	0.033	0.024		0.022	8
	Shafter	<0.010	<0.010	0	<0.010	0		<0.010	8
	Bakersfield	0.040	0.010	6	0.015	0.012	-	0.010	30
Backgd sites	Fresno	0.020	0.020	10	0.015	0.003		0.015	39
	Sacramento	0.010	0.010	2	0.010	0		0.010	28
STUDY 2	Heber	0.092	0.078	9	0.033	0.030	0.028	0.018	14
	Holtville	0.029	0.015	7	0.017	0.008		0.014	13
	Brawley Swing School	0.040	0.033	8	0.021	0.011		0.018	13
Imperial Valley	Brawley APCD Trailer	0.035	0.026	12	0.019	0.007		0.017	14
	Calipatria-1	0.150	0.046	8	0.044	0.044		0.024	13
	Calipatria-2	0.044	0.041	8	0.031	0.011		0.033	12
Backgd site	El Centro	0.014	0.010	2	0.012	0.003	-	0.012	14

a Mean and median values of samples positive for ethyl parathion only (# above MDL).

TABLE 7 SUMMARY OF AMBIENT AIR CONCENTRATIONS OF ETHYL PARATHION AND ETHYL PARAOXON CONVERTED TO ETHYL PARATHION IN 24-HOUR SAMPLES in parts per trillion (ppt)

	Location	Highest Value	Second Highest Value	# Above MDL	Mean[a]	±SD	Overall Mean[a]	Median[a]	Total # of Samples
STUDY 1	Sanger	16.05	8.24	7	6.03	5.15	**14.09**	6.02	11
	Parlier-1	**117.50**	99.41	12	25.72	39.12		8.90	13
Northern	Parlier-2	13.56	13.00	10	7.74	4.53		7.30	10
San Joaquin	Reedley	62.84	41.95	13	21.27	18.16		14.47	13
Valley	Dinuba	31.09	24.00	13	11.21	9.66		6.98	13
	Selma	22.91	21.64	8	12.62	6.93		11.89	13
	Earlimart	5.04	4.16	2	4.60	0.62	3.03	4.60	6
	Delano-1	1.29	1.24	2	1.26	0.04		1.26	7
Southern	Delano-2	<0.80	<0.80	0	<0.80	0		0.80	5
San Joaquin	McFarland	7.34	6.04	5	3.53	2.97		2.13	7
Valley	Wasco	5.69	1.98	4	2.72	1.99		1.85	8
	Shafter	<0.80	<0.80	4	<0.80	0		0.80	8
	Bakersfield	3.40	0.84	6	1.27	1.01	-	0.10	30
Backgd sites	Fresno	1.70	1.70	10	1.27	0.01		1.24	39
	Sacramento	0.84	0.84	2	0.84	0		0.84	28
STUDY 2	Herber	7.6	6.4	9	2.7	2.5	2.25	1.9	14
	Holtville	2.4	2.2	7	1.4	0.63		1.2	13
	Brawley Swing School	3.3	2.7	8	1.7	0.90		1.5	13
Imperial	Brawley APCD								
Valley	Trailer	2.9	2.1	12	1.5	0.55		1.4	14
	Calipatria-1	12.0	3.8	8	3.6	3.50		2.3	13
	Calipatria-2	3.5	3.4	8	2.6	0.87		2.7	12
Backgd site	El Centro	1.2	0.8	2	1.0	0.30	-	1.0	14

a Mean and median values of samples positive for ethyl parathion only (# above MDL).

Imperial Valley when ethyl parathion is applied in late summer. Acccordingly, the ARB performed two field studies at the times of highest use in those two areas.

B. Study 1: San Joaquin Valley, January 6 to February 14, 1986

1. Description of Study

The usage rates and typical application areas reported in the 1983 pesticide use report and historical meteorological data from local airports were entered into the EPA's Industrial Source Complex Short Term Air Quality Model by the ARB staff to determine the locations of expected highest short-term concentrations of ethyl parathion (see Section II. Background, E. Use of Models to Estimate Air Levels of Ethyl Parathion).

The study was divided into two time frames since historical data indicated that application times differed between the northern and southern portions of the San Joaquin Valley. In the northern San Joaquin Valley, the study was carried out over 23 days, mostly in January (Table 8A-C), whereas in the southern San Joaquin Valley, the study was carried out over 16 days in February (Table 8D).

Based on the results of the modeling study, ten sampling locations in Fresno, Tulare and Kern counties were chosen. Specific site locations were chosen according to their proximity to possible application areas,

considerations of safety and security, permission for the use of the site, and availability of electrical power. Background sampling was done in Fresno (Fresno County), Bakersfield (Kern County) and Sacramento (Sacramento County) from January through April 1986. Low volume samplers, fitted with XAD-2 resin adsorbants, were used to collect air samples at approximate rates of 1.7 to 2.6 liters per minute (lpm) for each of the 24 hour samples. One sampler was placed at each site except at Parlier and at Delano where two samplers were located. At the single sampler site locations, 24 hour samples were to be collected 4 times per week. At Parlier and Delano, two samples were collected during each 24 hour period (or 8 samples/week) for the determination of sampling precision. Additionally, in an attempt to quantify peak exposure, a third sampler was used to collect 3-hour samples once or twice a day from 13 January through 16 January 1986 at Parlier and from 3 February through 6 February 1986 at Delano.

The samplers were positioned in accordance with the U.S. EPA Ambient Air Quality Monitoring, Data Reporting, and Surveillance Provisions 40 CFR 58, Ambient Air Quality Surveillance, Appendix E, Probe Siting Criteria for Ambient Air Quality Monitoring. They were generally located 12 to 23 feet above ground level and 50 yards to one mile from agricultural fields. Neither meteorological nor parathion use information were obtained for the sampling sites over the period of study. After collection, the samples were capped, stored on wet ice, delivered to the

laboratory and analyzed within two weeks of collection by the method described in Appendix I.2.

2. Results - Study 1

The observed ethyl parathion concentrations at San Joaquin Valley sites are listed in Table 8A-D. Seventy-six of 133 test samples collected (57%) contained detectable levels of ethyl parathion. The highest 24-hour value measured was 1.423 $\mu g/m^3$ (117.50 ppt) at Parlier. The site-specific average for samples positive for ethyl parathion ranged from below the MDL (0.01 $\mu g/m^3$ or 0.8 ppt) at Shafter to 0.314 $\mu g/m^3$ (25.72 ppt) at Parlier. The mean of all samples positive for ethyl parathion at all sites during the study period was 0.170 $\mu g/m^3$ (14.09 ppt) in the northern San Joaquin Valley and 0.037 $\mu g/m^3$ (3.03 ppt) in the southern San Joaquin Valley. No ethyl parathion was detected in the three-hour samples. Ninety-seven samples were collected at the three background sites. Of these, 18 had ethyl parathion at detectable levels (0.01 to 0.04 $\mu g/m^3$, 0.8 ppt to 3.4 ppt, data not shown).

Paraoxon, the primary active degradation product, was detected in 6 samples collected in the northern San Joaquin Valley, at levels between MDL (0.02 $\mu g/m^3$ or 1.6 ppt) and 0.069 $\mu g/m^3$ (6.0 ppt) (Table 8B). Paraoxon levels in the 6 samples were converted to parathion equivalent values, weighted for its increased toxicity and added to the measured parathion values in those samples (Table 8C).

TABLE 8A AMBIENT AIR MONITORING OF ETHYL PARATHION

Study 1: 24-Hour Field Samples - Northern San Joaquin Valley

Date	Day	Sanger		Parlier 1		Parlier 2		Reedley		Dinuba		Selma	
		µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt
1-7-86	1	<0.010	<0.8	0.069	5.69	0.066	5.45	0.051	4.16	0.036	2.94	<0.010	<0.8
1-8-86	2	<0.010	<0.8	0.025	2.14	0.025	2.14	0.040	3.33	0.071	5.89	<0.010	<0.8
1-9-86	3	-	-	<0.010	<0.8	0.016	1.38	0.035	2.85	0.034	2.82	<0.010	<0.8
1-13-86	7	<0.010	<0.8	0.080[a]	6.62	0.058	4.82	0.142	11.73	0.069	5.73	<0.010	<0.8
1-14-86	8	-	-	0.140[a]	11.58	0.066	5.44	0.124	10.29	0.375	31.09	0.277	22.91
1-15-86	9	0.022	1.85	0.071[a]	5.82	0.113	9.42	0.186	15.38	0.289	24.00	0.045	3.78
1-16-86	10	0.100	8.24	0.080[a]	6.69	0.111	9.14	0.160	13.27	0.109	7.93	<0.010	<0.8
1-21-86	15	0.193	16.05	0.157	9.85	0.157	13.0	0.410	34.0	0.084	6.98	0.155	12.87
1-22-86	16	0.027	2.20	0.096	7.96	0.157	13.0	0.275	22.91	0.069	5.78	0.104	8.65
1-23-86	17	0.016	1.38	0.224	18.54	0.164	13.56	0.175	14.47	0.073	6.11	0.069	5.67
1-27-86	21	0.073	6.02	0.834[b]	69.09	-	-	0.358[b]	29.64	0.035	9.67	0.175	14.54
1-28-86	22	<0.010	<0.8	0.693[b]	57.45	-	-	0.277[b]	22.91	0.156[b]	12.96	0.260	21.64
1-29-86	23	0.078	6.45	0.204	16.85	-	-	0.227[b]	18.91	0.109	9.02	0.131	10.91
	n	7	7	12	12	10	10	13	13	13	13	8	8
c	x	0.073	6.03	0.223	18.19	0.093	7.74	0.189	15.68	0.116	10.07	0.152	12.62
	SD	0.062	5.15	0.261	21.71	0.055	4.53	0.118	9.78	0.103	8.33	0.084	6.930
	n	11	11	13	13	10	10	13	13	13	13	13	13
d	x	0.050	4.65	0.206	16.85	0.093	7.74	0.189	15.68	0.116	10.07	0.097	8.07
	SD	0.058	4.90	0.257	21.34	0.055	4.53	0.118	9.78	0.103	8.33	0.096	7.99
	n	11	11	13	13	10	10	13	13	13	13	13	13
e	x	0.048	3.88	0.206	16.82	0.093	7.74	0.189	15.68	0.116	10.07	0.095	7.92
	SD	0.059	4.98	0.257	21.36	0.055	4.53	0.118	9.78	0.103	8.33	0.098	8.14

a On this date, 3-hour samples were taken. None of these samples contained detectable levels of ethyl parathion.
b Paraoxon was detected in these samples.
c Mean value of samples positive for ethyl parathion only.
d Mean value of all samples using a minimum detectable level (MDL) of 0.01 µg/m³ or 0.8 ppt.
e Mean value of all samples using a MDL of 0.005 µg/m³or 0.4 ppt.

12/1/87

TABLE 8B. AMBIENT AIR MONITORING OF ETHYL PARAOXON

Study 1: 24-Hour Field Samples - Northern San Joaquin Valley

Date	Day	Sanger		Parlier 1		Parlier 2		Reedley		Dinuba		Selma	
		µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt
1-7-86	1	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-8-86	2	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-9-86	3	-	-	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-13-86	7	<0.02	<1.6	<0.02[a]	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-14-86	8	-	-	<0.02[a]	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-15-86	9	<0.02	<1.6	<0.02[a]	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-16-86	10	<0.02	<1.6	<0.02[a]	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-21-86	15	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-22-86	16	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-23-86	17	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6	<0.02	<1.6
1-27-86	21	<0.02	<1.6	0.035	3	-	-	0.014	1	<0.02	<1.6	<0.02	<1.6
1-28-86	22	<0.02	<1.6	0.069	6	-	-	0.042	4	0.017	1	<0.02	<1.6
1-29-86	23	<0.02	<1.6	<0.02	<1.6	-	-	0.024	2	<0.02	<1.6	<0.02	<1.6
	n	0	0	2	2	0	0	3	3	1	1	0	0
b	x	<0.02	<1.6	0.052	4.50	<0.02	<1.6	<0.027	2.33	0.017	1	<0.02	<1.6
	SD	0	0	0.024	2.12	0	0	0.014	1.53	0	0	0	0

a On this date, 3-hour samples were taken. None of these samples contained detectable levels of ethyl paraoxon.

b Mean values of samples positive for ethyl paraoxon only.

12/1/87

TABLE 8C. AMBIENT AIR CONCENTRATIONS OF ETHYL PARATHION AND ETHYL PARAOXON CONVERTED TO ETHYL PARATHION

Study 1: 24-Hour Field Samples - Northern San Joaquin Valley

Date	Day	Sanger		Parlier 1		Parlier 2		Reedley		Dinuba		Selma	
		µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt
1-7-86	1	<0.010	<0.8	0.069	5.69	0.066	5.45	0.051	4.16	0.036	2.94	<0.010	<0.8
1-8-86	2	<0.010	<0.8	0.025	2.14	0.025	2.14	0.040	3.33	0.071	5.89	<0.010	<0.8
1-9-86	3	-	-	<0.010	<0.8	0.016	1.38	0.035	2.85	0.034	2.82	<0.010	<0.8
1-13-86	7	<0.010	<0.8	0.080[a]	6.62	0.058	4.82	0.142	11.73	0.069	5.73	<0.010	<0.8
1-14-86	8	-	-	0.140[a]	11.58	0.066	5.44	0.124	10.29	0.375	31.09	0.277	22.91
1-15-86	9	0.022	1.85	0.071[a]	5.82	0.113	9.42	0.186	15.38	0.289	24.00	0.045	3.78
1-16-86	10	0.100	8.24	0.080[a]	6.69	0.111	9.14	0.160	13.27	0.109	7.93	<0.010	<0.8
1-21-86	15	0.193	16.05	0.157	9.85	0.157	13.0	0.410	34.0	0.084	6.98	0.155	12.87
1-22-86	16	0.027	2.20	0.096	7.96	0.157	13.0	0.275	22.91	0.069	5.78	0.104	8.65
1-23-86	17	0.016	1.38	0.224	18.54	0.164	13.56	0.175	14.47	0.073	6.11	0.069	5.67
1-27-86	21	0.073	6.02	1.204[b]	99.41	-	-	0.508[b]	41.95	0.035	9.67	0.175	14.54
1-28-86	22	<0.010	<0.8	1.423[b]	117.50	-	-	0.761[b]	62.84	0.336[b]	27.74	0.260	21.64
1-29-86	23	0.078	6.45	0.204	16.85	-	-	0.477[b]	39.39	0.109	9.02	0.131	10.91
	n	7	7	12	12	10	10	13	13	13	13	8	8
c	x	0.073	6.03	0.314	25.72	0.093	7.74	0.257	21.27	0.130	11.21	0.152	12.62
	SD	0.062	5.15	0.473	39.12	0.055	4.53	0.220	18.16	0.120	9.66	0.084	6.93

a On this date, 3-hour samples were taken. None of these samples contained detectable levels of ethyl paraoxon.

b This value represents the sum of ethyl parathion and ethyl paraoxon converted to ethyl parathion.

c Mean value of samples positive for ethyl parathion only.

TABLE 8D AMBIENT AIR MONITORING OF ETHYL PARATHION

Study 1: 24-Hour Field Samples - Southern San Joaquin Valley

Date	Day	Shafter		Wasco		McFarland		Delano-1		Delano-2		Earlimart	
		µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt
1-28-86	1	<0.010	<0.8	0.069	5.69	0.089	7.34	<0.010	<0.8	-	-	0.051	4.16
1-29-86	2	<0.010	<0.8	0.020	1.71	0.073[a]	6.04	0.016[b]	1.29	-	-	0.060	5.04
2-03-86	7	<0.010	<0.8	<0.010	<0.8	0.007[a]	0.65	<0.010[b]	<0.8	<0.010	<0.8	<0.010	<0.8
2-05-86	9	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8	<0.010[b]	<0.8	<0.010	<0.8	<0.010	<0.8
2-06-86	10	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8	<0.010[b]	<0.8	<0.010	<0.8	<0.010	<0.8
2-10-86	14	<0.010	<0.8	<0.010	<0.8	0.016	1.49	<0.010	<0.8	<0.010	<0.8	-	-
2-11-86	15	<0.010	<0.8	0.024	1.98	0.025	2.13	0.015	1.24	<0.010	<0.8	<0.010	<0.8
2-12-86	16	<0.010	<0.8	0.018	1.51	-	-	-	-	-	-	-	-
	n	0	0	4	4	5	5	2	2	0	0	2	2
c	x	<0.010	<0.8	0.033	2.72	0.042	3.53	0.016	1.26	<0.005	<0.4	0.056	4.6
	SD	0	0	0.024	1.99	0.037	2.97	0.001	0.04	0	0	0.006	0.62
	n	8	8	8	8	7	7	7	7	5	5	6	6
d	x	<0.010	<0.8	0.021	1.76	0.033	2.75	0.012	0.93	<0.010	<0.8	0.025	2.07
	SD	0	0	0.020	1.66	0.034	2.76	0.003	0.23	0	0	0.024	1.98
	n	8	8	8	8	7	7	7	7	5	5	6	6
e	x	0.005	0.4	0.019	1.38	0.031	2.63	0.008	0.65	0.005	0.4	0.022	1.8
	SD	0	0	0.022	1.94	0.035	2.86	0.005	0.42	0	0	0.026	2.19

a Date of sample collection was 4 February 1986.
b On this date, 3-hour samples were taken. None of these samples contained detectable levels of ethyl parathion.
c Mean value of samples positive for ethyl parathion only.
d Mean value of all samples using a minimum detectable level (MDL) of 0.01 µg/m³ or 0.8 ppt.
e Mean value of all samples using a MDL of 0.005 µg/m³ or 0.4 ppt.

C. Study 2: Imperial Valley, September 23 through October 22, 1986

1. Description of Study

Using the same criteria as described for Study 1, six sampling locations within Imperial County were chosen: five field sites and one background site at El Centro. A single sampler was located at each site except for Calipatria, where two samplers were located. Low volume systems were used to collect measured air samples of 24-hour duration at rates of 2 to 4 lpm. Each sample represented a total sample volume of between 4002 and 5300 liters.

Samples were collected 4 times per week at each site. Samplers were located 14 to 30 feet above ground level and 100 yards to 0.5 miles from fields that could be sprayed. The samples were sealed, stored on wet ice, shipped to the laboratory, and analyzed within two weeks of collection using the method described in Appendix III.G.2.

As for Study 1, no parathion use information was obtained for the sampling sites over the period of study. However, local meteorological observations were made.

2. Results - Study 2

The measured concentrations of ethyl parathion in samples collected in the Imperial Valley are listed in Table 9. At the test sites, 52 of a total of 79 samples (66%) contained detectable levels of ethyl parathion. The highest individual value observed was 0.15 $\mu g/m^3$ (12 ppt) in Calipatria. The mean concentration for samples positive for ethyl parathion during the 24-day study period ranged from 0.017 $\mu g/m^3$ (1.4 ppt) at Holtville to 0.044 $\mu g/m^3$ (3.6 ppt) at Calipatria. The mean for all the samples positive for ethyl parathion collected at all the sites during the study period was 0.028 $\mu g/m^3$ (2.25 ppt). Paraoxon was not detected in any of the field samples collected. Out of 14 samples analyzed from the background site, two contained detectable levels of ethyl parathion, with an average background level of 0.010 $\mu g/m^3$ (0.83 ppt) for all 14 samples.

D. Discussion

Figures 2 through 4 depict the reported use of ethyl parathion during the periods of study in those counties where monitoring was carried out. Both Kern County in the southern San Joaquin Valley and Imperial County reported approximately equally low levels of use, whereas Fresno County in the northern San Joaquin Valley reported relatively higher levels. These higher use rates seem to have resulted in higher atmospheric levels

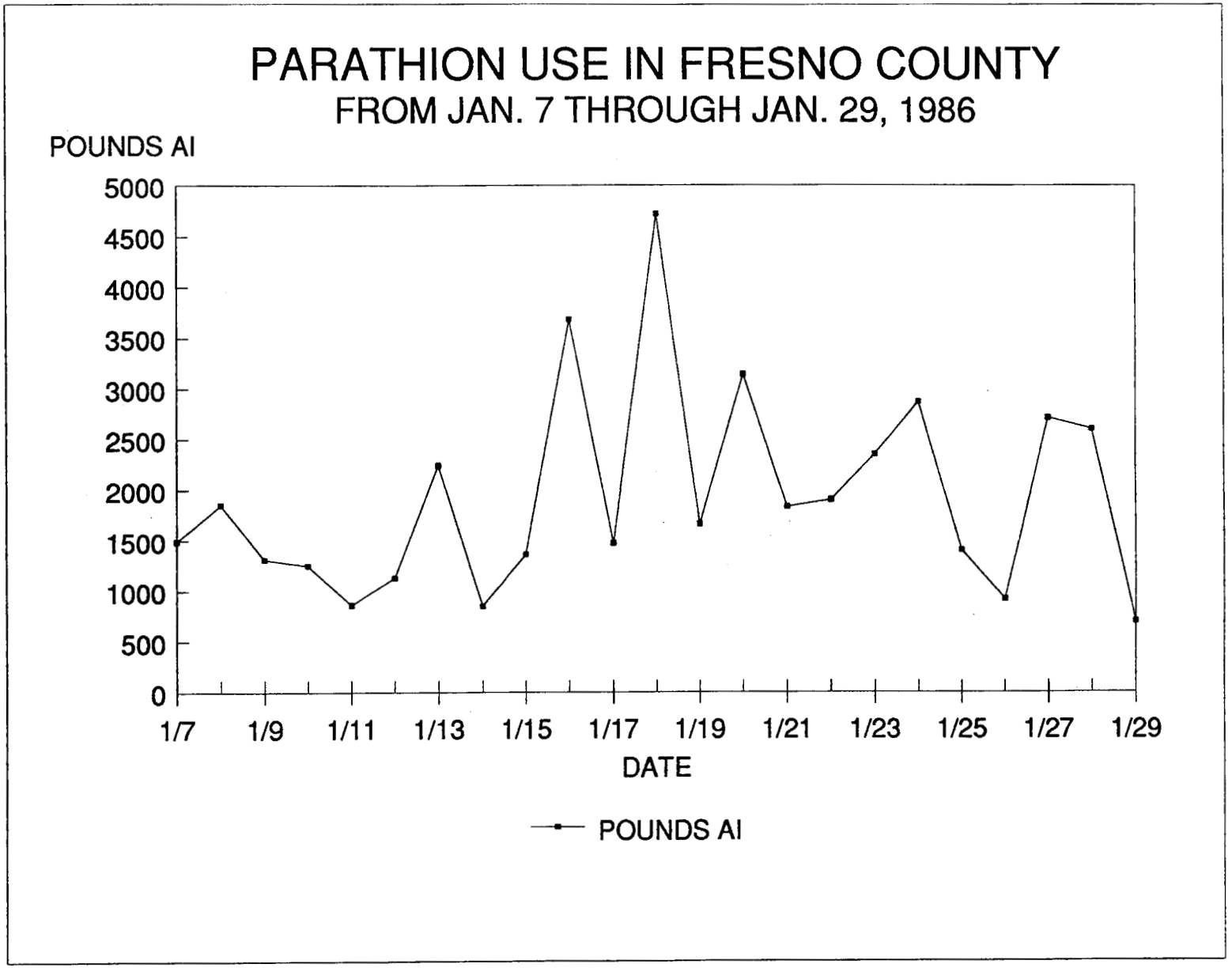
TABLE 9 AMBIENT AIR MONITORING OF ETHYL PARATHION

Study 2: 24-Hour Field Samples - Imperial Valley

Date	Day	Heber		Holtville		Brawley Swing School		Brawley APCD Trailer		Calipatria-1		Calipatria-2		El Centro[a]	
		µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt	µg/m³	ppt
9-29-86	1	<0.010	<0.8	0.029	2.4	0.033	2.7	0.035	2.9	0.022	1.8	0.028	2.3	<0.010	<0.8
9-30-86	2	<0.010	<0.8	0.013	1.0	0.040	3.3	0.014	1.2	0.020	1.6	0.022	1.8	<0.010	<0.8
10-01-86	3	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8	0.014	1.2	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8
10-02-86	4	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8	0.015	1.2	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8
10-06-86	8	0.018	1.5	0.009	0.8	<0.010	<0.8	0.019	1.6	0.150	12.0	-	-	<0.010	<0.8
10-07-86	9	0.032	2.6	0.029	2.2	0.016	1.3	0.022	1.8	0.046	3.8	0.044	3.5	0.014	1.2
10-08-86	10	0.012	1.0	-	-	0.022	1.8	0.026	2.1	0.037	3.1	0.038	3.1	0.010	0.8
10-09-86	11	0.015	1.2	0.015	1.2	-	-	0.014	1.2	-	-	-	-	<0.010	<0.8
10-14-86	16	<0.010	<0.8	<0.010	<0.8	0.017	1.4	0.015	1.2	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8
10-15-86	17	0.078	6.4	0.013	1.1	0.020	1.6	0.020	1.6	0.022	1.8	0.026	2.2	<0.010	<0.8
10-16-86	18	0.092	7.6	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8
10-20-86	22	0.023	1.9	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8	<0.010	<0.8	0.013	1.1	<0.010	<0.8
10-21-86	23	0.018	1.5	<0.010	<0.8	<0.010	<0.8	0.010	0.8	0.025	2.0	0.041	3.4	<0.010	<0.8
10-22-86	24	0.010	0.9	0.014	1.2	0.008	0.7	0.021	1.7	0.031	2.6	0.039	3.3	<0.010	<0.8
	n	9	9	7	7	8	8	12	12	8	8	8	8	2	2
b	x	0.033	2.7	0.017	1.4	0.021	1.7	0.019	1.5	0.044	3.6	0.031	2.6	0.012	1.0
	SD	0.030	2.5	0.008	0.6	0.011	0.9	0.007	0.55	0.044	3.5	0.011	0.9	0.003	0.3
	n	14	14	13	13	13	13	14	14	13	13	12	12	14	14
c	x	0.025	2.0	0.014	1.1	0.017	1.4	0.018	1.4	0.031	2.52	0.024	1.99	0.010	0.83
	SD	0.026	2.2	0.007	0.5	0.010	0.8	0.007	0.6	0.037	3.01	0.014	1.12	0.001	0.11
	n	14	14	13	13	13	13	14	14	13	13	12	12	14	14
d	x	0.023	1.9	0.012	0.9	0.015	1.2	0.016	1.4	0.029	2.36	0.023	1.86	0.006	0.49
	SD	0.028	2.3	0.009	0.7	0.012	1.0	0.008	0.7	0.039	3.11	0.016	1.28	0.003	0.23

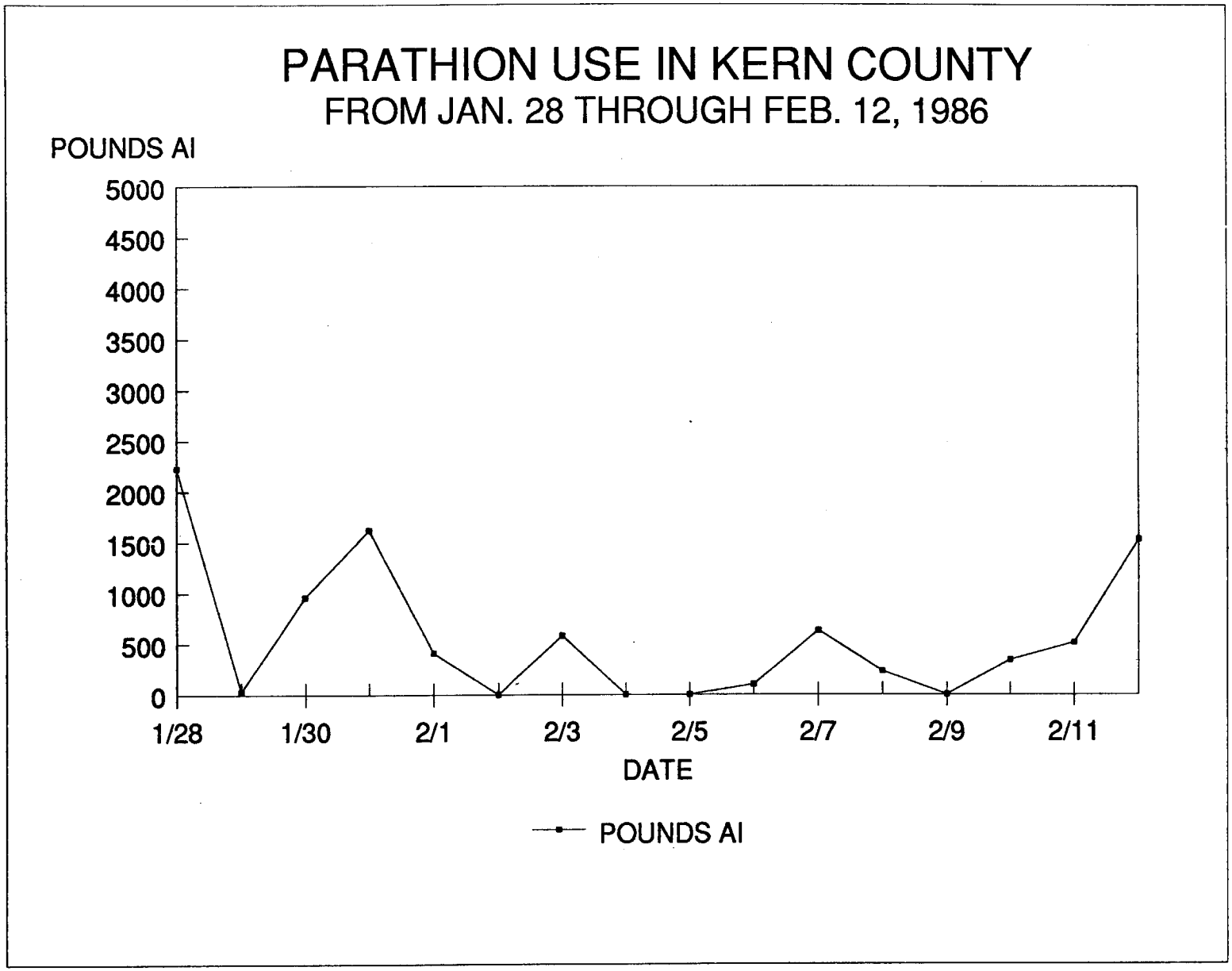
a Background site
b Mean value of samples positive for ethyl parathion only.
c Mean value of all samples using a minimum detectable level (MDL) of 0.01 µg/m³ or 0.8 ppt.
d Mean value of all samples using a MDL of 0.005 µg/m³ or 0.4 ppt.

Figure 2.



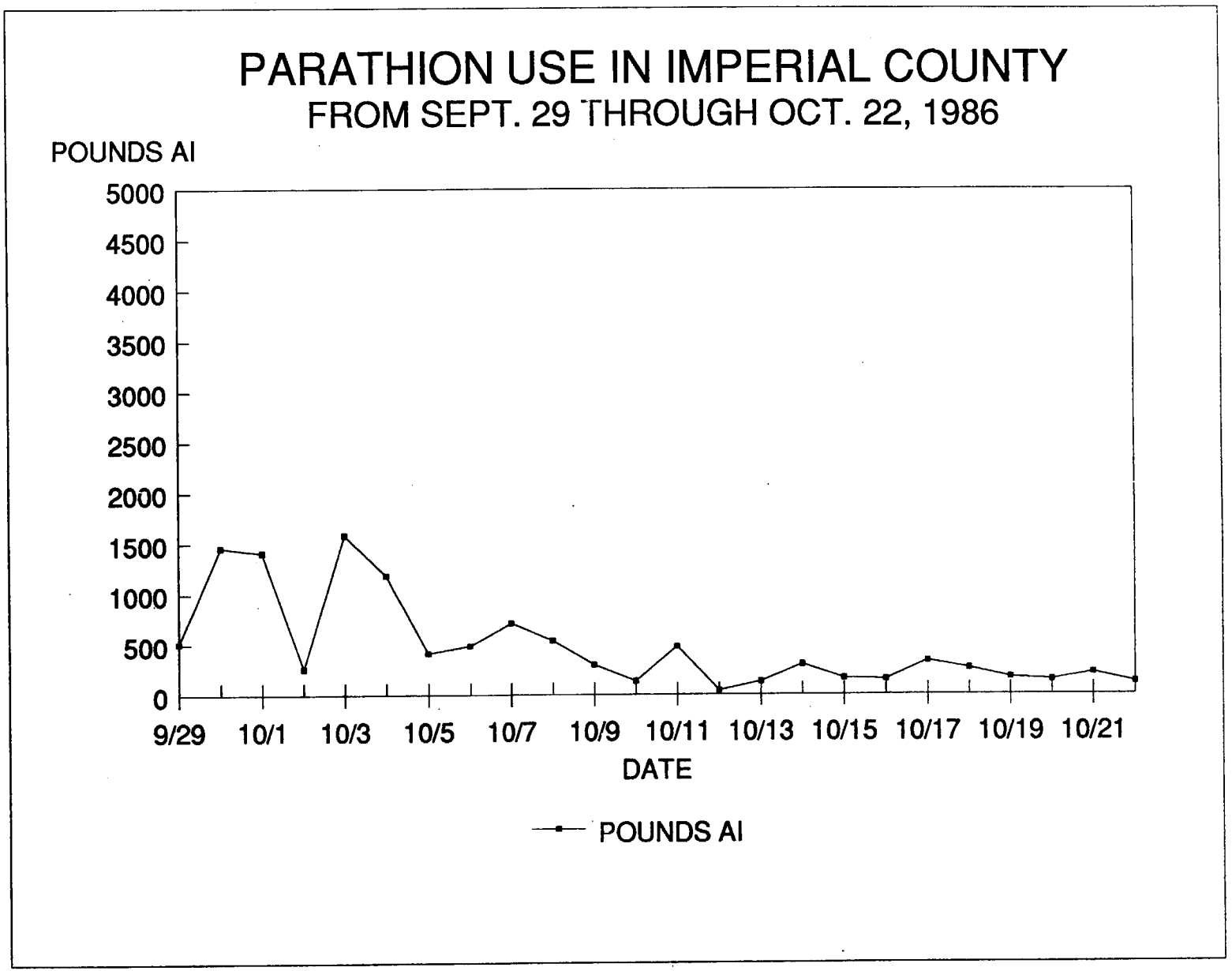
From: CDFA Pesticide Use Report, 1986

Figure 3.



From: CDFA Pesticide Use Report, 1986

Figure 4.



From: CDFA Pesticide Use Report, 1986

of ethyl parathion in the San Joaquin Valley compared to those airborne levels measured in the Imperial Valley.

If monitoring had taken place near an application site, it was determined that a 20-minute sample would have detected 1 $\mu g/m^3$, assuming a method MDL of 0.01 $\mu g/m^3$ and a flow rate of 2 liters/minute (ARB, personal communication). However, the 3-hour ambient air monitoring at Parlier and Delano did not detect measurable levels of ethyl parathion. This suggests that actual application did not take place during those intervals, the interval was too short to trap enough ethyl parathion to exceed the detection limits, or flow rates were too low to accumulate measurable residues. Thus, peak short-term exposure values are not available.

The presence of paraoxon in some of the samples collected in the San Joaquin Valley study is due to oxidative conversion of parathion in the environment or within the sampler tube (Woodrow et al., 1977). As part of their quality control procedures, the ARB spiked sample tubes with parathion, analyzed the samples for both parathion and paraoxon and reported an average conversion rate of less than 6 percent. The values for paraoxon measured in the field varied from four to 15 percent of the parathion values in the same samples, with four of six samples containing levels of paraoxon greater than 6 percent of the measured level of parathion. These results suggest that in those four samples, the portion

of the paraoxon measured above artifact levels may be atmospheric in origin.

Because paraoxon is more toxic than parathion, paraoxon levels should be converted back to parathion equivalent values, weighted to reflect the increased toxicity, and added to the parathion levels measured in the same samples. Based on the data presented in Table 11, it was determined that paraoxon is ten times as toxic as parathion. Therefore, paraoxon was converted to parathion equivalent values, those values were increased by a factor of ten, and then added to the parathion levels (Table 8C).

That paraoxon was detected in so few samples taken in the San Joaquin Valley (Study 1) was most likely due to the wet winter weather, since environmental conversion of ethyl parathion has been shown to be dependent upon the presence of heat, sunlight, atmospheric pollutants and high dust levels (Nigg et al., 1979; Spear et al., 1978). In the Imperial Valley (Study 2), samples were collected in the late summer. But since measured concentrations of ethyl parathion were exceedingly low, any conversion to paraoxon may not have been detected.

The CDFA monitored air levels in the Imperial Valley at the same time Study 2 was being carried out by the ARB (see Table 5D). The overall mean for all sites monitored by the CDFA was 0.040 $\mu g/m^3$ which is approximately 40% higher than the overall mean (0.028 $\mu g/m^3$) of the values obtained by the ARB. Whereas 66% of the samples collected by the

ARB contained detectable levels of parathion, 95% of the samples collected by the CDFA were positive for parathion. These slightly higher values and greater number of positive samples were probably due to the greater volume of air/sample collected by the CDFA. The CDFA study results suggest that low ambient air levels of ethyl parathion may be relatively widespread over rural areas during periods of high use.

In summary, the ambient air values of parathion reported in the central valley and Imperial Valley are within the range of values reported in other studies and tabulated in Table 5D.

E. Quality control

Because of heavy fog conditions in the San Joaquin Valley during the sampling period for Study 1, there was concern over the effectiveness of the sampling system to detect organophosphate pesticides. Tests showed that the presence of heavy fog had no effect on the ability of the sampling system to detect organophosphates.

Quality control procedures were followed and included assessment of method sensitivity, precision, accuracy, desorption efficiencies and sample stability. For both studies, the ARB determined that the average MDL for the analytical method used was 0.01 $\mu g/m^3$ (0.8 ppt) for ethyl parathion and 0.02 $\mu g/m^3$ (1.6 ppt) for paraoxon. The coefficent of variation, defining the sampling precision (or variability) between

samples collected at the same site, averaged 17% for Study 1 (San Joaquin Valley) and 11% for Study 2 (Imperial Valley). The methodology used to determine sampling precision is described in the U.S. EPA guidelines, Title 40, Code of Federal Regulations, Section 58. Chain-of-custody procedures were followed to ensure traceability of the samples.

A flow rate discrepancy was discovered in Study 1 in which the actual flow was found to be 55% to 86% of the indicated flow. Therefore, correction factors were used to determine ambient concentrations of ethyl parathion. The values reported here have been corrected (Table 6, 8). For Study 2, the sampling system was redesigned, and the indicated and true flow rates were within 1 percent of each other.

Desorption or trapping efficiencies, calculated by spiking the sampling tube in the laboratory with increasing concentrations of ethyl parathion and then analyzing the samples, varied between 84 and 92 percent for ethyl parathion and 94 to more than 100 percent for paraoxon. No field spikes were done for Study 1. In Study 2, the percent recovery of ethyl parathion in field-spiked samples was calculated and found to be between 86 and 98 percent.

A study was performed to assess the stability of ethyl parathion over time. The results showed that if the sample was refrigerated, the concentration of pesticide in the sample was stable over a two-week period.

F. Population at Risk

Whereas Table 4 presents the rural population of those counties where the most ethyl parathion is used, Table 10 presents specific information about the monitoring sites including the distance of the samplers from fields, the counties in which the sites were located, the rural population of the monitoring sites, and the highest 24-hour values measured at those sites. There does not seem to be a correlation between the highest values of parathion measured and distance from fields that may have been sprayed. For example, the highest value of 1.423 $\mu g/m^3$ was measured at a site 440 yards from the nearest fields despite the fact that there were several other samplers located as close as 50 yards from fields. Under worst case circumstances, in the northern San Joaquin Valley, as many as 47,000 persons could be exposed to as much as 0.170 $\mu g/m^3$ of atmospheric ethyl parathion over the study period of one month. Additionally, as shown in Table 4 and 10, most of the sites for the northern San Joaquin Valley study were located in Fresno County, which has the highest rural population of the top ten users of ethyl parathion. In the southern San Joaquin Valley and the Imperial Valley, 43,000 and 24,000 persons could be exposed to much lower levels of 0.037 $\mu g/m^3$ and 0.028 $\mu g/m^3$, respectively.

TABLE 10 CHARACTERIZATION OF MONITORING SITES AND MEASURED AMBIENT AIR CONCENTRATIONS AT THOSE SITES

	County	Site	Population [a]	Distance from Fields (yds)	Highest Value Parathion µg/m³	Total Population	Overall Mean [b] µg/m³
STUDY 1							
Northern San Joaquin Valley	Fresno	Sanger	12,542	N 150 E 1,760	0.193		
	Fresno	Parlier	2,902	N 440 S 440 E 440 W 440	1.423		
	Fresno	Reedley	11,071	SE 50 S 440	0.761		
	Tulare	Dinuba	9,907	W 587 S 50	0.375		
	Fresno	Selma	10,942	N 50 S 50 E 50	0.277		
						47,364	0.170
Southern San Joaquin Valley	Tulare	Earlimart	4,578	E 220	0.060		
	Kern	Delano	16,491	E 440 W 220	0.015		
	Kern	McFarland	5,151	W 440	0.089		
	Kern	Wasco	9,613	NW 440	0.069		
	Kern	Shafter	7,010	W 440	<0.010		
						42,843	0.037
STUDY 2							
Imperial Valley	Imperial	Heber	2,221	W 200	0.092		
	Imperial	Holtville	4,399	N 100 S 100 E 100 W 100	0.029		
	Imperial	Brawley	14,946	W 880	0.040		
	Imperial	Calipatria	2,636	N 440 W 440	0.150		
						24,202	0.028

a 1980 U.S. Census
b Mean of samples positive for ethyl parathion

G. Estimate of Current Airborne Levels

Because no peak short-term concentrations were obtained from these monitoring studies, acute levels were selected from the literature. The 15-20 minute sample of 34 $\mu g/m^3$ measured during application and the 2-hour sample value of 3.09 $\mu g/m^3$ measured immediately after application were chosen for margin of safety determinations (Table 5C, Maddy et al. 1983). These air concentrations were selected from a study conducted in California during and after an application made under relatively current regulations governing ethyl parathion use. In addition, the time periods over which the samples were taken were specifically reported.

The 24-hour value of 1.423 $\mu g/m^3$ (117.50 ppt) at Parlier on 28 January 1986 was the highest level measured at any site in Study 1 and 2 over either study period (Table 6 and 7). Therefore, this airborne concentration was used in estimating risk following acute ambient exposure.

When comparing the results of monitoring in the northern San Joaquin Valley, the southern San Joaquin Valley and the Imperial Valley, the highest mean value of all samples positive for ethyl parathion was 0.170 $\mu g/m^3$ (14.09 ppt) in the northern San Joaquin Valley (Study 1) (Table 6 and 7). This mean value represents all sites monitored in the northern San Joaquin Valley over a 3-week period in January. Thus, 0.170 $\mu g/m^3$

(14.09 ppt) was used as the ambient air concentration from which risk following sub-chronic exposure was estimated.

The value of 0.170 $\mu g/m^3$ (14.09 ppt) was also used in estimating risk following chronic exposure.

H. References

Nigg, H.N., Allen, J.C., King, R.W. 1979. Behavior of parathion residues in the Florida "Valencia" orange agroecosystem. J. Agric. Food Chem. 27:578-582.

Spear, R.C., Lee, Y-S., Leffingwell, J.T., Jenkins, D. 1978. Conversion of parathion to paraoxon in foliar residues: effects of dust level and ozone concentration. J. Agric. Food Chem. 26:434-436.

Woodrow, J.E., Seiber, J.N., Crosby, D.G., Moilanen, K.W., Soderquist, C.J., Mourer, C. 1977. Airborne and surface residues of parathion and its conversion products in a treated plum orchard environment. Arch. Environm. Contam. Toxicol. 6:175-191.

I. Appendices

1. Equations used:

$$\mu g/m^3 = \frac{\text{amount of pesticide } (\mu g)}{\frac{[\text{flow rate } (l/min)][\text{sampling period } (min)]}{1000\ l/m^3}}$$

$$ppt = \frac{24.05 \times \mu g/l \times 10^6}{M.W.}$$

at 294^oK (68^oF) and 760 mm Hg (1 atm) where 24.05 is the gas constant or $l.atm/mol.^oK$

I. **Appendices (cont.)**

2. ARB Method ADDL003 - Method for the Determination of Selected Organophosphate Pesticides in Ambient Air.

2. ARB Method ADDL003

METHOD ADDL003

METHOD FOR THE DETERMINATION OF
SELECTED ORGANOPHOSPHATE PESTICIDES IN AMBIENT AIR

1. Scope

This document describes a method for the sampling and analysis of parathion, methyl parathion, paraoxon, malathion, and diazinon at concentrations normally found in ambient air. The method was developed based on NIOSH, EPA and the California Department of Food and Agriculture published methods.

2. Summary of Method

After sampling using a low-volume system comprising pump, controller, glass fiber pre-filter, and purified XAD-2 absorbant trap, the exposed filter and absorbant are desorbed with 2.0 milliliters of 80/20 isoctane/acetone mixture. Two micoliters of the extract are injected using splitless mode technique into a gas chromatographic system equipped with a 30 meter DS-5 capillary column, thermionic detector (TSD), and data system. The resultant peaks are identified by characteristic retention times and quantitated in reference to external standards. The identity of a component may be confirmed by use of a column with different characteristics, a second detector system, or by GC/MS.

3. Interferences/Limitations

3.1 Components having similar GC retention times will interfere, causing misidentification and/or erroneous quantitation.

3.2 Extreme care must be taken to insure that sample losses do not occur due to leaks in the sampling system or to sample handling within the laboratory. All glassware must be throughly cleaned to insure that cross-contamination does not occur between samples. Samples are to be protected from sunlight during sampling and storage.

4. Apparatus

4.1 Varian Model 3300 Gas Chromatograph equipped with thermionic detector (TSD) and a Vista 402 Data System.

4.2 DB-5 fused silica capillary column, 30 meters x 0.35 mm i.d., 1µm film thickness.

4.3 Amber vials, 3.7 ml capacity, with teflon-lined septum caps.

4.4 Sample agitator with timer and sample rack.

4.5 Microliter syringes, 5-50 µl sizes

4.6 Low-volume sampler pump and flow controller capable fo maintaining preset flow rates of 6 lpm over a 24 hour period. Sampling system must have an accurate timer system to control sampling interval and to indicate total sampling elasped time.

4.7 Sampling head capable of containing a 37 mm glass fiber filter in-line with a 6" x 1/4" absorption tube containing XAD-2 absorbant.

4.8 Glass fiber filters, 37 mm diameter, type A/E, with teflon holder.

4.9 Glass absorption tubes, 6" x 1/4", containing purified XAD-2 absorbant; 400 mg primary section, 200 mg secondary section. Absorbant must be demonstrated to be free of interfering substances by analysis of unused absorbants (analytical blanks).

5. Reagents

5.1 80/20 iso-octane/acetone desorbant solvent: Mix 50 ml pesticide grade iso-octane (trimethyl pentane) and 20 ml pesticide grade acetone in a clean glass bottle equipped with teflon-lined screw cap. CAUTION: Flammable - DO NOT expose to heat or oxidizers.

5.2 Stock Standards: Individual 1000 µg/ml certified stock standards containing diazinon, parathion, methyl parathion, malathion, and paraoxon may be obtained from Nanogens, Inc. CAUTION: Toxic - Use protective gloves in handling these materials.

5.3 Working Standards: Dilute 20 µl of each stock standard into 50/50 isoctane/acetone solvent and dilute to 10.0 ml. This corresponds to 2.0 µg/ml standard.

6. Instrument Conditions

Column: 30 m x 0.37 mm i.d. DB-5 fused silica capillary column

Temperature - Injector: 250°C
Detector: 300°C
Oven: 50°C, initial, hold for 1 minute, ramp at 50°C/min to 140°C/min; ramp at 4°C/min to 260°C, 4 min hold

Flow Rates: Carrier - He, 60 cc/min at splitter, 0.5 min splitless hold, carrier velocity after splitter opens: 25 cm/sec

Detector: TSD - Range 11, Attenuation x 32
Hydrogen Flow: 4.5 cc/min
Air Flow: 180 cc/min
Heater: 3.4 amp

7. Sample Collection

7.1 Sampling flow controllers and indicators must be calibrated by trained personnel before the unit can be installed in the field. The flow rate calibration must be verified monthly at the flow rate used for sampling.

7.2 The 37 mm glass fiber filter and holder, as received from the laboratory, is placed in the sampling head compartment. The compartment is then assembled, taking care that the unit is completely sealed. The filter holder may be handled, but care must be taken not to touch or contaminate the filter itself. If any question of contamination is present, the filter is discarded and a new filter is installed.

7.3 The sealed XAD-2 absorbant tube is prepared for use by snapping off the sealed ends with the tool provided. The open tube is then placed in the sampling train using 1/4" polyethylene tubing fittings, making sure that the flow indicator arrow printed on the tube points in the direction of the flow. The tubing fittings must be tightened sufficiently to insure that the system is leak-free.

7.4 After starting the pump system, the flow must be adjusted to approximately 6 lpm. The time, indicated flow reading, and the true flow (read from the calibration graph) must be recorded. The filter and absorbant trap numbers must be recorded. The elapsed time meter is reset to zero. The system is leak-checked by sealing the sampler inlet and insuring that the flow is zero.

7.5 After a 24 hour sampling period, the indicated flow and true flow rates must be recorded. The sampler system is deactivated, the elapsed time and actual time is recorded, and the filter and absorbant tube removed. The filter and cassette holder is placed into a plastic shipping container. The tube is sealed using the red end caps provided. The filter and tube are immediately sent to the laboratory with all sampling information and chain of custody.

8. Instrument Calibration Procedure

8.1 Before a standard solution may be injected, a system blank must be analyzed. This is done by injecting 2.0 µl of 80/20 iso-octane/ acetone solvent for analysis. If the subsequent analysis indicates interferences or contamination, the solvent must be replaced.

8.2 A method blank must be analyzed for every 10 samples. This is done by randomly selecting a "blank" (unused) filter and absorbant tube, desorbing (extracting) the "blank" filter and absorbant, and injecting 2.0 µl of the resultant extract into the instrument for analysis. If interferences or contamination is noted, the source must be found and, if possible, eliminated.

8.3 Instrument calibration is performed by injection of 2.0 µl of 2.0 µg/ml mixed standard. The resultant chromatogram and calculated concentrations must be inspected to insure proper integration and consistency with previous analyses. The data is then used to calibrate the method. The instrument data system will not accept updated response factors which are not within 10 percent of historic data.

8.4 If the analyses are to be made daily, a weekly analysis of three standards (2.0, 0.4, 0.08 µg/ml) must be made to insure that the method exhibits linear response. In addition, a weekly "spiked" sample of 0.8 micrograms per absorbant tube of individual pesticides must be taken through the entire analytical scheme to insure that the method is in control. The results of these analyses must be entered on the method control charts.

9. Analysis of Samples

9.1 After removal of the glass fiber filter from the teflon filter holder using stainless steel forceps, the filter is carefully rolled and placed in a 3.7 ml vial. The filter must be forced into the bottom of the vial to insure that the entire filter is in contact with the solvent.

9.2 After removal of the red end-caps from the absorbant tube, the tube is scored using a glass cutter above the location of the retainer spring. Using the tool provided, the tube is then broken and the retainer spring removed. The glass wool plug and the primary (400 mg) section of XAD-2 is placed in a 3.7 ml vial. Similarly, the secondary section (200 mg) of XAD-2 is placed in a second vial. Make sure all vials are properly identified.

9.3 Place 2.0 ml desorbing solvent (80/20) into the vials, cap tightly and place on vial agitator for 45 minutes.

9.4 After desorption, 2.0 µl of each extract is injected into the chromatographic system for analysis. The data generated from the glass fiber filter extract is recorded as "filterable". The combined results are recorded as "total".

9.5 The results are recorded in micrograms/m^3 and are calculated as follows:

$$\mu g/m^3 = \frac{\mu g/ml \text{ (found)} \times 2 \times 1000}{\text{average flow (lpm)} \times \text{time sampled (minutes)}}$$

10. Method Sensitivity, Precision, and Accuracy

10.1 The method sensitivity, precision, and accuracy are outlined in Table I. The data was generated using standards.

11. Desorption Efficiencies and Sample Stability

11.1 The primary section of the XAD-2 sampling tube was "spiked" with 10 µl of solutions containing known amounts of the five organophosphate pesticides of interest. The tubes were then sealed, placed in a refrigerator for storage, and tested after intervals to test the stability of the materials on the sorbant. Table II presents the results of this study. Note that the samples are stable for over a period of two weeks.

11.2 The primary section of the XAD-2 sampling tube was "spiked" with 10 µl of solutions containing known amounts of the five pesticides of interest. The "spiked" tubes were then placed in the low volume sampling device and sampled at a flow rate of 7.5 lpm for differing lengths of time. Both the primary and secondary sections of the sampling tubes were desorbed and analyzed. The results are presented in Table III. Note that at the sampling rate of 7.5 lpm, the breakthrough volume of all the pesticides tested is greater than 14 m^3.

Table I

Compound	Conc. 1 µg/ml	S.D.* (percent)	Conc. 2 µg/ml	S.D. (percent)	Conc. 3 µg/ml	S.D. (percent)	MDL µg/ml
Diazinon	2.0	11.6	0.4	14	0.06	7	0.04
Methyl Parathion	2.0	2.3	0.4	8	0.08	7	0.02
Paraoxon	2.0	11	0.4	12	0.08	11	0.04
Malathion	2.0	9.6	0.4	10	0.08	8	0.04
Parathion	2.0	8.3	0.4	8	0.08	9	0.02

Compound	Correlation Coefficient	Slope	Intercept (µg/ml)
Diazinon	0.998	0.980	0.031
Methyl Parathion	0.998	0.988	0.016
Paroxon	0.997	0.996	0.026
Malathion	0.997	0.991	0.032
Parathion	0.998	1.003	-0.015

S.D. = Relative Standard Deviation

Table II

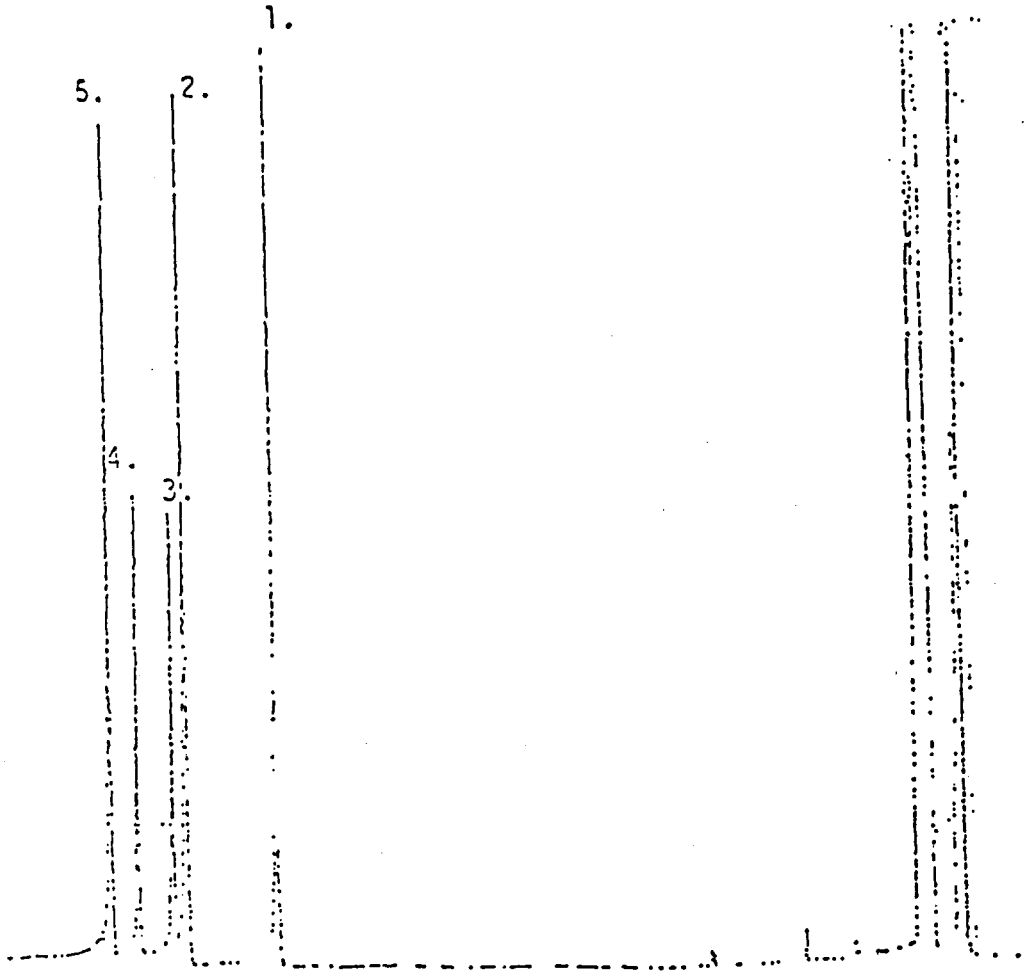
ORGANO-PHOSPHATE PESTICIDE STABILITY STUDY

Storage Time, Hrs:	0	24	48	96	192	384
Compound	Amount Recovered, µg (Percent)					
Diazinon	1.68 (98)	1.60 (93)	1.70 (99)	1.58 (92)	1.64 (95)	1.62 (94)
Methyl Parathion	1.45 (83)	1.42 (82)	1.50 (86)	1.40 (80)	1.42 (82)	1.35 (78)
Paroxon	1.42 (97)	1.40 (96)	1.48 (101)	1.38 (94)	1.40 (96)	1.41 (96)
Malathion	1.42 (91)	1.38 (88)	1.50 (96)	1.40 (90)	1.42 (91)	1.48 (96)
Parathion	1.50 (88)	1.52 (89)	1.60 (94)	1.46 (86)	1.50 (88)	1.42 (84)

Table III

ORGANO-PHOSPHATE PESTICIDE SAMPLING AND BREAKTHROUGH STUDY

Volume Sampled (m^3) (7.5 lpm)	3.6	7.2	10.8	14
Compound	Amount Recovered, µg (percent) Primary/µg (percent) Secondary			
Diazinon	1.60 (93)/0 (0)	1.66 (96)/0 (0)	1.56 (91)/0 (0)	1.92 (100)/0 (0)
Methyl Parathion	1.47 (84)/0 (0)	1.55 (89)/0 (0)	1.44 (83)/0 (0)	1.62 (93)/0 (0)
Paroxon	1.40 (96)/0 (0)	1.48 (101)/0 (0)	1.38 (94)/0 (0)	1.50 (103)/0 (0)
Malathion	1.44 (93)/0 (0)	1.48 (95)/0 (0)	1.40 (90)/0 (0)	1.50 (96)/0 (0)
Parathion	1.52 (89)/0 (0)	1.55 (92)/0 (0)	1.42 (84)/0 (0)	1.56 (92)/0 (0)



STANDARD: 1.0 µg/ml Mixed Standard
CONDITIONS: DB-6 Capillary Column, 30m, 50°C(1 min.), 50°C/min to 140°C, 4°C/min to 260°C(4 Min.); TSD, 3.4 A, Range 11; Helium carrier, 26 cm/sec, splitless.

1. Diazinon
2. Methyl Parathion
3. Paraoxon
4. Malathion
5. Parathion

IV. HEALTH EFFECTS AND RISK ASSESSMENT

Ethyl parathion (commonly referred to as parathion) is an organophosphate insecticide whose mode of action is inhibition of acetylcholinesterase. This inhibition accounts for most of the resulting toxicity. Parathion is extremely toxic following acute exposures and has been implicated in a large number of occupational poisonings (EPA, 1986). Considering the toxicity of parathion and the widespread use, there is considerable concern over its short and long term effects to human health. The first part of this section is a review of the currently available health effects data for parathion, followed by an assessment of its potential impact on human health at ambient air concentrations.

A. Hazard Identification

1. Mechanism of Action

Parathion produces most of its toxic reactions by the inhibition of acetylcholinesterase (AChE) (Hayes, 1982; Murphy, 1986; Taylor, 1985). These effects are associated with paraoxon, the metabolic oxygen analog, rather than parathion itself. Paraoxon reacts at the active site of AChE, thereby inhibiting the breakdown of acetylcholine (ACh). Initially, paraoxon is bound reversibly to AChE, but over time the compound undergoes aging and becomes irreversibly bound. Acetylcholine is the chemical transmitter of nerve impulses at preganglionic to postganglionic neurons of

both parasympathetic and sympathetic nervous systems, postganglionic parasympathetic fibers to effector organs, postganglionic sympathetic fibers to sweat glands, motor nerves to skeletal muscles, and some nerve endings in the central nervous system (CNS). Acute parathion intoxication is manifested by muscarinic and nicotinic symptoms, as well as CNS symptoms. These effects include headaches, nausea, vomiting, cramps, diarrhea, weakness, blurred vision, pin-point pupils, tightness in the chest, labored breathing, nervousness, sweating, lacrimation, salivation, muscle spasms, coma and death. The cause of death is due primarily to respiratory failure. Atropine and 2-pyridine aldoxime methiodide (2-PAM) are used as specific antidotes for parathion poisoning. Atropine antagonizes the action of acetylcholine at the muscarinic receptor, whereas 2-PAM reactivates acetylcholinesterase if the phosphorylated enzyme has not undergone aging.

In addition to the interaction with acetylcholinesterase, paraoxon also inhibits butyrocholinesterase (BuChE or pseudo-ChE). This inhibition, however, produces no apparent functional derangement. In this document, cholinesterase used in general terms will refer to both acetylcholinesterase and pseudo- or butyrocholinesterase, whereas plasma cholinesterase will refer to pseudo- or butyrocholinesterase. The cholinesterase associated with other tissues (i.e. RBC and brain) is acetylcholinesterase (AChE). Cholinesterase inhibition in whole blood, plasma or red blood cells (RBC) is the most frequently used index of parathion-induced toxicity. Following an acute exposure, plasma ChE activity can return to normal within several days after exposure. RBC AChE

will remain inhibited for the life of the erythrocyte and, hence, these values can remain depressed for an extended period (Murphy, 1986).

2. Pharmacokinetics

a. Routes of Exposure and Absorption

Parathion is a lipophilic organophosphate compound which is readily absorbed by all routes of exposure. It is rapidly absorbed from the gut following oral administration (Agarwal et al., 1982; Newell and Dilley, 1978; Owens, 1977). The half-time for absorption in the mouse has been estimated at 33 minutes, and by 60 min, 58% of the dose was absorbed (Ahdaya, et al., 1981). The cumulative excretion of radiolabelled parathion over a five day period in the dog indicated that 78% of the oral dose was absorbed and the time to maximum concentration in the plasma was estimated at 3.5 hours (Braeckman et al., 1983).

Parathion is absorbed by the lungs in animals and humans (Atallah et al., 1975; Durham et al., 1972; Hartwell et al., 1964; Hartwell and Hayes, 1965; Newell and Dilley, 1978; Nye and Dorough, 1976; Owens, 1977; Richter et al., 1980; and Simpson, 1973). Hartwell and coworkers (1964, 1965) have demonstrated significant toxic effects in humans following inhalation exposure, as well as a decreased incidence of parathion-induced symptoms when respirators were introduced as a protective measure into a work force. Nearly complete absorption was reported in volunteers exposed to parathion mists (Durham et al., 1972). Nye and Dorough (1976) found close to 100% absorption of parathion in female rats following endotracheal administration of the pesticide. Additionally, when Newell and Dilley

(1978) converted LC_{50} (1 hr exposure, mg/m^3) to mg/kg for rats, the doses were comparable to the intravenous injection (i.v.) LD_{50} (5.14 mg/kg inhalation; 6.40 mg/kg i.v.).

Dermal absorption of parathion has been extensively investigated (Bronaugh, 1985; Durham et al., 1972; Feldman and Maibach, 1974; Fisher et al., 1985; Funckes et al., 1963; Hayes et al., 1964; Knaak et al., 1984; Knaak and Wilson, 1985; Maibach, et al., 1971; Murphy, 1980; Nabb et al., 1966; Newell and Dilley, 1978; Reifenrath et al., 1984a, 1984b; Riley, 1983; Shah and Guthrie, 1977, 1983; Shih et al., 1985; Skinner and Kilgore, 1982a, 1982b; Wolfe et al., 1967), and it is considered to be the primary route of exposure in the occupational setting (Durham et al., 1972; NIOSH, 1976; Ware et al., 1973; Wolfe et al., 1967). Since it is not a dermal sensitizer, the skin may be contaminated unknowingly for extended periods of time (Rycroft, 1977). Percutaneous absorption of parathion has been shown to be a function of the area exposed, concentration on the skin and length of exposure (Knaak et al., 1984; Knaak and Wilson, 1985; Hayes et al., 1964). Additionally, site of exposure (Maibach et al., 1971; Skinner and Kilgore, 1982a, 1982b) and temperature (Funckes et al., 1963; Hayes et al., 1964) affect the dermal absorption of parathion. Unlike other routes of exposure, percutaneous absorption varies greatly across species. The rabbit has been reported to absorb nearly 100% of an applied dose over 24 hours (Shah and Guthrie, 1977), the rat absorbed approximately 60% over 120 hours (Knaak et al., 1984), while absorption in humans has been estimated between 10-30% over 24 hours (Feldman and Maibach, 1974; Maibach et al.,

1971; Reifenrath et al., 1984b; Shah and Guthrie, 1983). With increased exposure time, however, more parathion would be absorbed.

b. Distribution

Parathion is rapidly and widely distributed throughout the body (Ahdaya et al., 1981; Eigenberg et al., 1983; Fredrikkson and Bigelow, 1961; Shah and Guthrie, 1977). Using whole body autoradiography in mice, Fredrikkson and Bigelow (1961) determined the distribution of a subcutaneous injection of ^{32}P-parathion equivalents at four hours post-exposure. The areas of highest radioactivity were salivary gland, fat, liver, and kidney, followed by lung, spleen, thyroid and gastrointestinal walls. Similar results were seen in the rabbit 24 hours after a topical application of ^{14}C-parathion (Shah and Guthrie, 1977). The tissues with the highest counts were lung, liver and kidney, and the counts were fairly evenly distributed across other tissues (i.e. brain, small and large intestines, heart and stomach). The particular affinity of parathion equivalents for the lungs in these studies may be important in acute exposures since respiratory failure is the primary cause of death (Taylor, 1985). Eigenberg and coworkers (1983) monitored parathion concentrations in the fat, brain, liver, plasma, and red blood cells following intravenous administration of the compound. These authors found a rapid distribution to these tissues, with some accumulation in the fat. Peak levels of parathion were observed in the brain within ten minutes, while parathion continued to increase in the fat for four hours. These authors also administered paraoxon intravenously to

rats and found rapid distribution to the brain, liver and red blood cells. Levels in the fat were not determined.

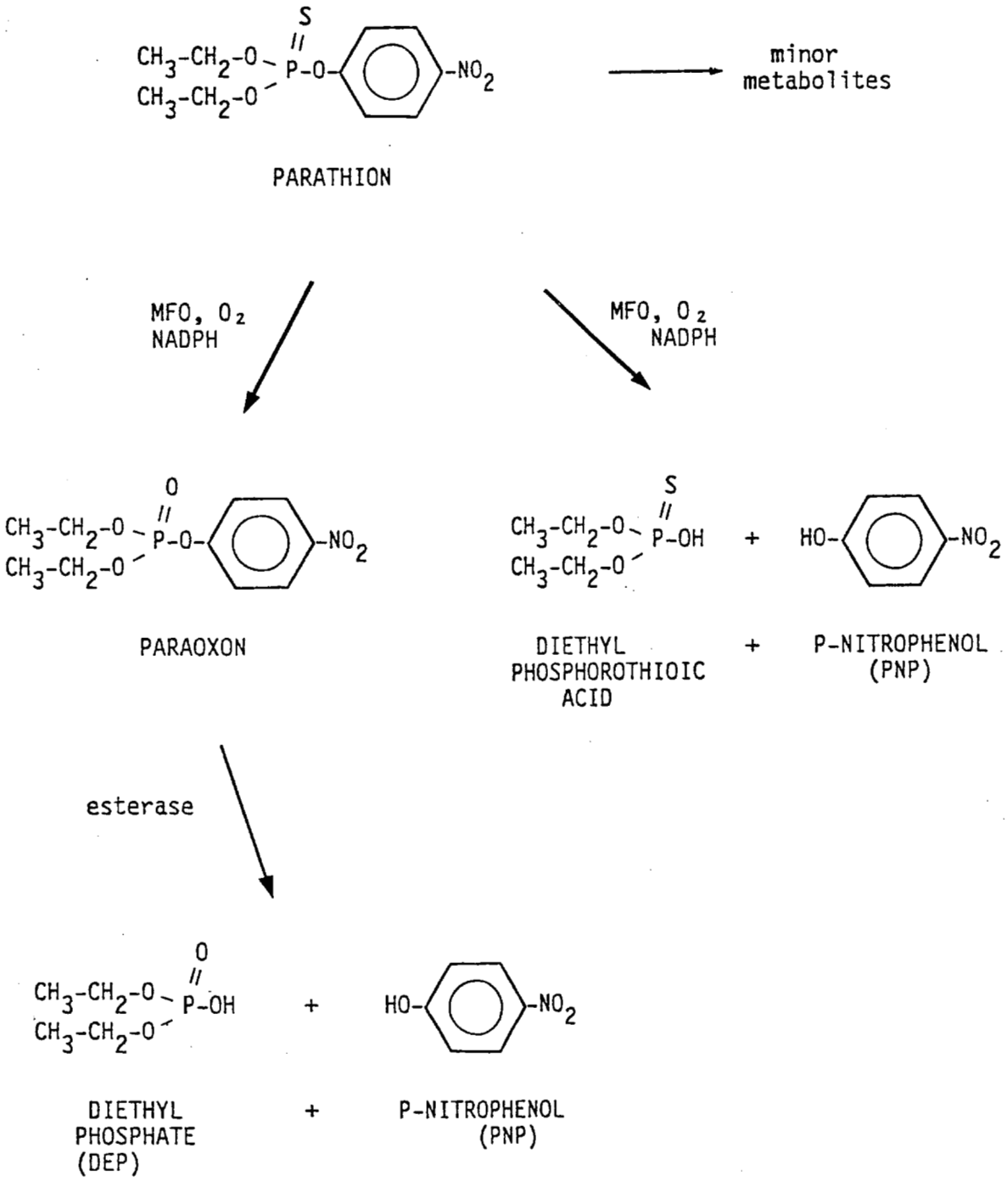
In addition to the wide organ distribution, parathion is bound extensively to plasma proteins (Braeckman et al., 1983; Maliwal and Guthrie, 1981; Mourik and de Jong, 1978; Skalsky and Guthrie, 1977, 1978; Sultatos et al., 1984). Protein binding has been demonstrated in the rat (Skalsky and Guthrie, 1977), dog, and human (Braeckman et al., 1983; Maliwal and Guthrie, 1981) and this binding was reversible (Mourik and de Jong, 1978; Sultatos et al., 1984). Parathion is bound to multiple sites in the albumin fraction of the serum proteins, although some additional binding to the lipoprotein fraction has been observed (Maliwal and Guthrie, 1981; Skalsky and Guthrie, 1978). Albumin has been reported to have a higher affinity for parathion than paraoxon, the active metabolite (Mourik and deJong, 1978).

c. Biotransformation

The major metabolic pathway of parathion is shown in Figure 1. Parathion undergoes oxidative desulfuration via the mixed function oxidase system to form paraoxon (Baker et al., 1979; Bradway et al., 1977; Dalvi and Howell, 1978; Fuhremann et al., 1974; Nakatsugawa et al., 1969; Neal and Halpert, 1982; Rao and McKinley, 1969). Paraoxon is the toxic metabolite which produces the anticholinesterase effects associated with parathion exposure. The metabolite is readily hydrolyzed by both microsomal and cytosolic esterases to form diethyl phosphate and p-nitrophenol. In addition, parathion can be hydrolyzed via a separate mixed

Figure 5.

METABOLISM OF PARATHION



function oxidase system to form diethyl phosphorothioic acid and p-nitrophenol. Other minor metabolites include the dealkylation products, ethyl phosphate and ethyl phosphorothioic acid. The metabolites of parathion are excreted principally in the urine (Fuhremann et al., 1974; Nakatsugawa et al., 1969). This metabolic pathway has been observed in a number of species including mouse (Sultatos et al., 1985), rat (Fuhremann et al., 1974), pig (Baker et al., 1979), chicken, monkey (Rao and McKinley, 1969), and man (Morgan et al., 1977; Shafik and Enos, 1969). Urinary p-nitrophenol has been used extensively as an index of occupational exposure to parathion (Arterberry et al., 1961; Durham et al., 1972; Funckes et al., 1963; Hartwell et al., 1964; Kuo et al., 1979).

While parathion undergoes considerable first pass metabolism in the liver (Baker et al., 1979; Braeckman et al., 1983; Sultatos et al., 1985), biotransformation to non-toxic metabolites is not complete, and paraoxon is present in the hepatic vein (Baker et al., 1979). In addition, parathion is metabolized by the lung, kidney, intestine, and brain, although to a much lesser extent than in the liver (Jacobson and Spear, 1973; Nakatsugawa et al., 1969; Neal, 1972; Norman and Neal, 1976; Nye and Dorough, 1976; Poore and Neal, 1972). Lung metabolism is the most significant extrahepatic metabolism and is estimated to be approximately 20% of liver metabolism. This metabolism may be an important factor in respiratory failure during acute toxicity (Jacobsen and Spear, 1973; Norman and Neal, 1976).

Pretreatment of mice and rats with phenobarbital had a protective effect against acute parathion toxicity. An increase in the intraperitoneal (i.p.) LD_{50} (Sultatos, 1986) and an increase in the ID_{50} (inhibition dose of cholinesterase; Murphy, 1980 a,b) were observed. Phenobarbital primarily induced the P-450 enzymes responsible for the initial metabolism of parathion, while the detoxifying esterases responsible for the breakdown of paraoxon were not changed. Sultatos (1986) hypothesized that the protective effects were largely due to the decrease in circulating parathion providing less substrate for extrahepatic metabolism at critical sites. Furthermore, parathion has been reported to induce some metabolic enzymes, although this effect on its overall metabolism is not known (Serban et al., 1979).

Inhibition of cytochrome P-450 has been observed following oxidative desulfuration, presumably from the covalent binding of sulfur to the enzyme (Halpert and Neal, 1980, 1982; Halpert et al., 1980; Morelli and Nakatsugawa, 1978; Seawright et al., 1976). While this phenomenon has been studied extensively in vitro, the doses of parathion used in vivo may not be sufficient to produce significant inhibition of the cytochrome P-450 (Halpert and Neal, 1980).

d. Kinetics

Parathion undergoes rapid metabolism and is excreted in the urine (Jenson et al., 1952). Twenty-four hours after human dermal exposures, the ^{14}C urinary metabolites were almost undetectable (Feldman and Maibach, 1974; Funckes et al., 1963; Morgan et al., 1977). Arterberry and

coworkers (1961) were able to detect ρ-nitrophenol 1-2 days after occupational exposure to parathion. Additionally, volunteers acutely exposed to parathion vapors had excreted most of the ρ-nitrophenol in their urine 24 hours after exposure (Hartwell et al., 1964). Similarly, rats exposed endotracheally (Nye and Dorough, 1976) or dermally (Shah and Guthrie, 1983) had eliminated most of the compound within 24 hours.

The kinetic fate of parathion and paraoxon in the dog and rat following intravenous injection were detailed by Eigenberg and coworkers (1983). The plasma decay curve for parathion was described by a multi-exponential equation, and the terminal $t_{1/2}$ for dog and the rat were 8.5-11.2 hours and 3.4 hours, respectively. The volumes of distribution (V_D) were large for both species (dog, 15-21 liters/kg; rat, 27 liters/kg), which was thought to be due to tissue distribution and plasma protein binding. Conversely, the paraoxon decay curve was mono-exponential, and the $t_{1/2}$ was estimated at 3.5 minutes in the rat. Paraoxon was rapidly broken down by esterases, and therefore did not accumulate. Braeckman et al. (1983) also found a multi-exponential kinetic curve for parathion in the dog. Using their data, the plasma $t_{1/2}$ appeared to be about 4 hours. The kinetics described in these studies were first order; however, zero-order kinetics were reported in two persons who ingested massive doses of parathion (approximately 15.4 mg/kg and 55.2 mg/kg; Kuo et al., 1979). The excretion curves remained zero-order for approximately 15 days, and ρ-nitrophenol was detected in the urine for over 25 days.

Finally, it should be noted that while parathion is rapidly metabolized and excreted under most exposure situations, plasma and RBC cholinesterase

inhibition may continue several weeks or more after exposure (Arterberry et al., 1961; Hartwell et al., 1964). Thus, urinary metabolites may not completely and accurately correlate with biological effects (Arterberry et al., 1961).

3. Acute Toxicity

The acute, lethal doses for parathion and paraoxon are listed in Table 11. Parathion is extremely toxic by all routes following acute exposure. The oral LD_{50} in rats ranges from 3.5 to 13 mg/kg. The female rat is more sensitive to parathion than the male; however, this sex difference has not been observed in other species. Lethal doses reported in humans are also presented. Background information on the dosages in adults was not available, while the child's dose was estimated from contaminated grain samples, not from blood or urine samples. Parathion has been classified by EPA as a Category I toxicant. Table 12 lists the values for cholinesterase inhibition (% of control) associated with acute parathion exposures in both animals and humans.

The most complete set of data is a series of studies on lethality and cholinesterase inhibition performed in the rat and dog using oral and inhalation routes of exposure for NIOSH at the Edgewood Arsenal (NIOSH, 1976; Owens, 1977). While the authors did not state how the inhalation studies were conducted, it is assumed that whole body exposure was used. The lethal threshold in the male rat following a single oral dose was 4 mg/kg and the calculated LD_{50} was 6.85 mg/kg. The oral lethal threshold dose for the male dog was 2.5 mg/kg and the LD_{50} was 8.27 mg/kg. The NOEL

TABLE 11
LD_{50} and LC_{50} VALUES FOR ETHYL PARATHION AND PARAOXON

Species	Sex	Route	Dose	Ref
Parathion:				
Rat	male	oral	$\bar{x}$= 7.6 mg/kg range= 2.04-30.0	1
Rat	female	oral	$\bar{x}$= 3.5 mg/kg range= 1.75-6.0	
Rat	male	oral	7.0 mg/kg	2
Rat	female	oral	2.6 mg/kg	
Rat	male	oral	2.7 mg/kg	3
Rat	female	oral	2.7 mg/kg	
Mouse	male	oral	$\bar{x}$= 23.0 mg/kg range= 7.0-30.3	1
Mouse	female	oral	$\bar{x}$= 12.7 mg/kg range= 6.0-25.0	
Dog	male	oral	8.27 mg/kg	4
Mouse	--	s.c.	10-12 mg/kg	10
Rat	male	i.p.	3.6-7.0 mg/kg	1
Rat	female	i.p.	4.0 mg/kg	
Mouse	male	i.p.	9-10 mg/kg	4
Rat	male	i.v.	6.4 mg/kg	5
Rat	female	i.v.	4.5 mg/kg	
Rat	male	inhalation, 1 hr inhalation, 4 hr	115 mg/m^3 31.5 mg/m^3	1
Rat	male	inhalation, 1 hr	1070 mg/m^3	5
Rat	female	inhalation, 1 hr	137 mg/m^3	
Rat	male	inhalation, 4 hr	84 mg/m^3	4
Rat	male	dermal	21.0 mg/kg	1
Rat	female	dermal	10.9 mg/kg	
Rat		dermal	50-200 mg/kg	
Rat	male	dermal	21.0 mg/kg	4
Rat	female	dermal	6.8 mg/kg	

TABLE 11, cont.

Species	Sex	Route	Dose	Ref
Rat	male	dermal	21.0 mg/kg	5
Rat	female	dermal	7.9 mg/kg	
Rat	male	dermal	49.4 mg/kg	
Rat	female	dermal	19.5 mg/kg	
Rabbit		dermal	0.07 ml/kg	1
Rabbit		dermal	40-50 mg/kg	
Rabbit		dermal	870 mg/kg	
Human	child	oral	0.1 mg/kg*	7
	adult	oral	2.1 mg/kg*	8
Human	adult	oral	0.24 mg/kg*	9
Paraoxon:				
Mouse	--	s.c.	0.6-0.8 mg/kg	10
Mouse	male	i.p.	2 mg/kg	12
Mouse	male	i.v.	0.52 mg/kg	
Mouse	male	oral	15 mg/kg	
Rat	--	oral	3 mg/kg	11
Rat	female	oral	1.8 mg/kg	13

* Not LD_{50}, but reported lethal doses.

References: 1. EPA 1975; 2. Auletta, 1984; 3. Terrell, 1979; 4. NIOSH, 1976; 5. Newell and Dilley, 1978; 6. Owens, 1977; 7. EPA, 1986; 8. Kanagartatnam, 1960; 9. ACGIH, 1986; 10. Holmstedt, 1963; 11. Kaemmerer and Buntenkotter, 1973; 12. Bass, et al., 1972; 13. Pickering and Malone, 1967.

TABLE 12
CHOLINESTERASE INHIBITION FOLLOWING ACUTE EXPOSURES

Species Sex	Route	Dose	Time Post Exposure	Cholinesterase Activity (% Control)		Ref
Rat male	oral	20 mg/kg	1 hr	blood	27%	1
				diaphragm	16%	
				muscle	70%	
				liver	45%	
				brain	49%	
				heart	39%	
Rat male	oral	20 mg/kg	3 hr	blood	7%	1
				diaphragm	5%	
				muscle	12%	
				liver	19%	
				brain	7%	
				heart	24%	
Rat male	i.p.	7.5 mg/kg	2 hr	plasma	5%	2
				RBC	8%	
			24 hr	plasma	5%	
				RBC	27%	
			3 days	plasma	17%	
				RBC	26%	
			5 days	plasma	93%	
				RBC	27%	
Rat male	i.p.	1 mg/kg	5 hr	RBC	50%	3
				brain	75%	
		1.5 mg/kg	"	RBC	50%	
				brain	75%	
		3 mg/kg	"	RBC	21%	
				brain	39%	
		5 mg/kg	"	RBC	15%	
				brain	25%	
Rat female (ED^{50})	dermal (neck/ back)	2.90 mg/kg	12 hr	brain	50%	4
		3.50 mg/kg	"	diaphragm	50%	
		1.45 mg/kg	"	plasma	50%	
		1.70 mg/kg	"	liver	50%	
	oral	1.73 mg/kg	1 hr	brain	50%	
		1.65 mg/kg	"	diaphragm	50%	
		1.15 mg/kg	"	plasma	50%	

TABLE 12, cont.

Species Sex	Route	Dose	Time Post Exposure	Cholinesterase Activity (% Control)		Ref
Dog male	inhalation (4 hrs)	0.015 mg/m^3	24 hr	plasma	14%	5
				RBC	49%	
		0.145 mg/m^3		plasma	20%	
				RBC	56%	
		3.42 mg/m^3		plasma	13%	
				RBC	44%	
		8.93 mg/m^3		plasma	7%	
				RBC	42%	
		37.1 mg/m^3		plasma	8%	
				RBC	45%	
Dog male	oral	0.5 mg/kg	24 hr	plasma	58%	5
				RBC	71%	
		1.26 mg/kg		plasma	60%	
				RBC	50%	
		2.50 mg/kg		plasma	41%	
				RBC	36%	
		10 mg/kg		plasma	35%	
				RBC	27%	
Rat male	inhalation (4 hr)	1.21 mg/m^3	24 hr	plasma	100%	5
				RBC	89%	
		2.17 mg/m^3		plasma	72%	
				RBC	70%	
		2.27 mg/m^3		plasma	42%	
				RBC	46%	
		12.8 mg/m^3		plasma	31%	
				RBC	42%	
Rat male	oral	0.35 mg/kg	24 hr	plasma	91%	5
				RBC	87%	
		0.70 mg/kg		plasma	77%	
				RBC	73%	
		1.40 mg/kg		plasma	55%	
				RBC	68%	
		2.80 mg/kg		plasma	66%	
				RBC	48%	

References: 1. Kemper, 1979; 2. Purshottam and Srivastava, 1984; 3. Murphy, 1969; 4. Murphy, 1980; 5. NIOSH, 1976 and Owens, 1977.

for RBC acetylcholinesterase inhibition in the male rat following acute inhalation (4 hour exposure) was 1.21 mg/m^3 (approx. 0.19 mg/kg) based on a biological threshold of 30% inhibition (Gage, 1976). The LOEL for this same effect was 2.17 mg/m^3 (approx. 0.35 mg/kg). Both of these are lower than the oral LOEL (lowest observed effect level) and NOEL (no observed effect level). The 4 hour inhalation study in the dog produced cholinesterase inhibition at extremely low concentrations (LOEL 0.015 mg/m^3, approx. 0.98 ug/kg). No NOEL was determined in this study. These data for the dog, however, appear to be inconsistent with other data presented in these studies. The inhalation LOEL is several orders of magnitude below the oral LOEL (0.5 mg/kg). Additionally, when dogs were exposed on a subchronic basis (7 hr/day, 5 day/wk, 6 wks) the cholinesterase NOEL was 0.01 mg/m^3 and the LOEL was 0.2 mg/m^3. Considering the discrepancies between these studies and the lack of confidence in the acute dog inhalation data, the NOEL for cholinesterase inhibition from the rat studies will be used for risk assessment.

Paraoxon was considerably more toxic than parathion by a factor ranging from 2 to 15, depending upon the route of administration. Paraoxon appeared to be least toxic when administered via the oral route, which may be due to extensive metabolism in the liver. The potency of paraoxon is estimated to be ten times greater than that of parathion, based on these data.

4. Subchronic and Chronic Toxicity

a. Subchronic Toxicity

Parathion has been tested in several species using both subacute and subchronic exposure protocols. Cholinesterase inhibition was the most frequently monitored parameter in these studies. A summary of these effects is presented in Table 13.

A series of studies in the rat and the dog were performed at the Edgewood Arsenal utilizing either oral or inhalation exposures over a six week period (NIOSH, 1976; Owens, 1977). Male rats were exposed to concentrations of parathion of 0.01, 0.1, or 0.74 mg/m^3 and male dogs were exposed to 0.001, 0.01, or 0.20 mg/m^3 for 7 hours/day, 5 days/week for 6 weeks. Since the method of inhalation exposure was not specified in these studies, it is assumed that whole body exposures were utilized. Oral exposures consisted of dosages of 0.05, 0.10, and 0.25 mg/kg in male rats and 0.05, 0.10, and 0.50 mg/kg in male dogs for 5 days/week for 6 weeks. Clinical symptoms and cholinesterase activities were the only effects assessed in these studies. Because statistical analyses were not performed on the data and standard deviations were not reported in the summary tables, cautious interpretation was required. The NOEL for cholinesterase inhibition in the rat appeared to be 0.01 mg/m^3. Plasma ChE was slightly depressed in the dog at 0.01 mg/m^3, but it was not inhibited at the earlier, weekly time points, nor was RBC AChE inhibited. Therefore, 0.01 mg/m^3 was designated as the NOEL for the dog in this study. The oral NOEL's for cholinesterase inhibition for the rat and the dog were 0.10 and

TABLE 13
CHOLINESTERASE INHIBITION FOLLOWING SUBCHRONIC EXPOSURE

Species, Sex	Exposure	Dose	Cholinesterase Activity (% Control)		Ref
Rat female	diet 11 days	2 ppm	plasma	93%	1
		2.5 ppm	"	96%	
		3 ppm	"	83%	
		3.5 ppm	"	72% *	
		4 ppm	"	72% *	
Rat female	diet 11 days	4 ppm	plasma	68% *	2
		8 ppm	"	35% *	
		12 ppm	"	32% *	
		16 ppm	"	35% *	
		20 ppm	"	23% *	
Rat female	diet 84 days	0.05 ppm	RBC	100%	3
		0.50 ppm	"	46% *	
		5.00 ppm	"	20% *	
Rat female	diet 90 days	2.5 ppm	plasma	94%	4
			RBC	44% *	
			brain	105%	
		25 ppm	plasma	52% *	
			RBC	47% *	
			brain	78% *	
		75 ppm	plasma	48% *	
			RBC	53% *	
			brain	40% *	
Rat male	diet 90 days	2.5 ppm	plasma	92%	4
			RBC	73%	
			brain	111%	
		25 ppm	plasma	75% *	
			RBC	47% *	
			brain	95%	
		75 ppm	plasma	75% *	
			RBC	33% *	
			brain	36% *	
Rat male	oral 5 d/wk 6 wks	0.05 mg/kg	plasma	156%	5 #
			RBC	115%	
		0.10 "	plasma	115%	
			RBC	81%	
		0.25 "	plasma	52%	
			RBC	46%	

TABLE 13, cont.

Species Sex	Exposure	Dose	Cholinesterase Activity (% Control)		Ref
Rat male	inhalation 7h/d, 5d/wk 6 wks	0.01 mg/m	plasma	99%	5 #
			RBC	97%	
		0.10 "	plasma	92%	
			RBC	67%	
		0.74 "	plasma	40%	
			RBC	26%	
Pig female	diet 33-122 days	0.2, 1.0, & 5.0 ppm	RBC	100%	3
		100 ppm	"	20% *	
Dog male and female	diet 5 months	1 ppm	plasma	95%	6
			RBC	80%	
		2 ppm	plasma	45% *	
			RBC	90%	
		5 ppm	plasma	40% *	
			RBC	60% *	
Dog male	oral 5d/wk 6 wks	0.05 mg/kg	plasma	54%	5 #
			RBC	83%	
		0.10 "	plasma	61%	
			RBC	80%	
		0.50 "	plasma	15%	
			RBC	42%	
Dog male	inhalation 7h/d, 5d/wk 6 wks	.001 mg/m	plasma	91%	5 #
			RBC	135%	
		.01 "	plasma	58%	
			RBC	101%	
		.20 "	plasma	36%	
			RBC	41%	
Baboon male and female	diet 2 yrs	0.15 mg/kg	blood	100%	7
			brain	100%	
		0.50 mg/kg	blood	74% *	
			brain	100%	
Human	oral 5 d/wk, 6wk	0.05 mg/kg	plasma	100%	8
			RBC	100%	
		0.12 mg/kg	plasma	63%	
			RBC	84%	
Human	oral 12 wks, last 3 wks at 0.05 mg/kg	0.05 mg/kg	RBC	100%	9

* Significantly depressed compared to controls at $p < 0.05$.
# Statistical significance not reported.

References: 1. Davies and Holub, 1978a; 2. Davies and Holub, 1978b; 3. Edson, 1964; 4. Daly, 1980b; 5. NIOSH, 1976 and Owens, 1977; 6. Frawley and Fuyat, 1957; 7. McGill, 1979. 8. Edson, 1964; 9. Rider et al., 1958.

0.05 mg/kg, respectively. Inhalation exposures in both species produced cholinesterase effects at lower equivalent doses than did oral exposures. The oral dosages convert into air concentrations which are over 10 fold greater than the actual inhalation exposures; although since it was assumed that the inhalation studies were whole body exposures, multiple routes of exposure (i.e. dermal, oral, and inhalation) cannot be ruled out.

Two rodent studies on file at California Department of Food and Agriculture assessed organ weights and histopathology following subchronic exposure. In the first study, male and female mice were fed parathion in concentrations of 0, 15, 50, or 100 ppm for 90 days (Daly, 1980a). Body weights were reduced in the high-dose males and in the mid- and high-dose females. No consistent organ weight changes were reported nor were gross or histopathological lesions observed. Cholinesterase activities were not measured. In a similar study, male and female rats were fed parathion at 0, 2.5, 25, or 75 ppm for 90 days (Daly, 1980b). The highest concentration (75 ppm) was particularly toxic to the females producing increased mortality and body and organ weight reductions (ovary, heart, kidney, and liver). While no weight changes or histopathological lesions were observed in the low-dose group, both males and females displayed decreased RBC AChE activities at this concentration (Table 13).

Adult male and female baboons were fed parathion (0.15 or 0.50 mg/kg/day; 3/sex/group) in diets containing high amounts of saturated fat and cholesterol (atherogenic diets) for 2 years (McGill, 1979). Neither dosage produced adverse effects in the cardiovascular system as assessed by blood chemistry and histopathology. No histopathologic lesions were

observed in other organs. Blood acetylcholinesterase activity was depressed in the high-dose group (74% of control) throughout most of the experiment. Brain AChE was not depressed, nor were blood and brain AChE's depressed in the low-dose group.

Effects on cholinesterase activity have been seen in both workers and volunteers following parathion exposure. Volunteers who ingested 7.2 mg/day (0.12 mg/kg/day), 5 days/week for 6 weeks, had significantly depressed RBC AChE (84% of control) and plasma ChE (63%; Edson, 1964), although no clinical symptoms were observed. Using additional exposure data, the author concluded that the NOEL for cholinesterase inhibition was 3 mg/day or 0.05 mg/kg/day based on an average 60 kg person. Rider and coworkers (1958) also found no decreases in RBC AChE in men and women volunteers who ingested increasing dosages of parathion over a 12 week period with the highest dose being 0.05 mg/kg/day for the final 3 weeks. No RBC or plasma cholinesterase changes were observed in 4 volunteers who ingested either 1 or 2 mg/kg of parathion for 5 days (Morgan et al., 1977). Workers, however, who were exposed to air concentrations between 1.4-2.0 mg/m^3 for up to 30 days had decreased plasma ChE values (21% decrease with a maximum reduction of 55%; Sassi et al., 1955). Six of the fifteen affected workers displayed clinical symptoms of poisoning. The possibility of dermal exposure, however, was not ruled out in this study.

b. Neurotoxicity

One of the major areas of concern with organophosphorus insecticides is the potential of these chemicals to induce peripheral neuropathies. This

neurotoxic effect has a delayed onset and is not attributable to the anticholinesterase properties of these insecticides; however, it has been attributed to the inhibition of neurotoxic esterase (NTE) activity. This syndrome begins several days or longer after exposure to an inducing agent and is manifested initially as mild sensory disturbances, ataxia and weakness in the legs. It may progress in severity to complete flaccid paralysis and may even involve the upper limbs. Recovery is slow and may not be complete. Humans and hens are more sensitive to delayed neuropathies than rodent species, and, hence, the hen is the preferred animal model for both in vivo and in vitro assays (Murphy, 1986).

Parathion has been studied extensively for delayed neuropathic effects in the hen and all reports have been negative. Following acute and subacute exposure, hens receiving a single dose at 10 mg/kg (p.o.), 50 or 100 ppm in diet for 3 days, or 2 mg/kg/day for 15 days in the feed did not exhibit any paralysis when monitored for up to 3 weeks after the end of exposure (Abou-Donia and Graham, 1979; Barnes and Denz, 1953; Soliman et al., 1982b). Furthermore, hens fed diets containing up to 1600 ppm parathion for 13-17 weeks, or hens exposed to 6 mg/kg/day either dermally or orally for 90 days did not develop delayed neuropathies (Frawley, 1976; Soliman et al., 1982a). In the latter study, there were no decreases in neurotoxic esterase activity nor were histological lesions observed in the spinal cord or sciatic nerve. A single dose of paraoxon (0.75 mg/kg) was administered to hens by gavage and no decreases in brain or lymphocyte NTE activity were seen, although a 56% decrease in brain AChE was observed (Schwab and Richardson, 1986). Since paraoxon has minimal NTE inhibitory

capabilities, it is used to inhibit the activity of nonspecific esterases in assaying for NTE (Hollingshaus and Fukuto, 1982).

In assessing delayed neurotoxicity in mammals, Soliman and coworkers (1982b) exposed male mice to parathion at a dosage of 6.75 mg/kg/day (p.o.) for 30 days. The authors observed no abnormal clinical signs or decreases in NTE activity. Male rats exposed to parathion at 2 mg/kg/day for 5, 10, or 15 days, or at 4 mg/kg for 5 days showed no change in sciatic nerve excitability 24 hours after the last dose (Averbook and Anderson, 1983). Recently, however, in a chronic feeding study submitted to the Department of Food and Agriculture, peripheral neuropathies were observed in male and female rats which received 50 ppm of parathion (Daly, 1984). These lesions were described as degeneration of the sciatic nerve. In a second chronic feeding study using male and female rats, no microscopic lesions were observed in the sciatic nerve with concentrations up to 32 ppm (Eiben, 1986). Both of these studies will be discussed in detail in the Chronic Toxicity section.

Parathion-induced delayed neurotoxicity has not been observed in humans except in a case study of a suicide attempt (deJager et al., 1981). The onset of polyneuropathy occurred 7 weeks after the incident and had abated by 1 year. Since the parathion was in a solution containing methyl alcohol, definitive conclusions could not be drawn concerning parathion.

In addition to the delayed neuropathies, transient myopathies have been observed, particularly in the diaphragm and soleus (Kibler, 1973; Wecker and Dettbarn, 1976; Wecker et al., 1978). These lesions are thought to be induced by excess ACh and were usually apparent within a few days of

administration of parathion. These lesions were reported to heal within a short period of time (one week to ten days) even with continued exposure. It has been proposed that tolerance or adaptation expressed as a refractoriness at the motor end plate to ACh is most likely involved with this phenomenon.

Behavioral effects consisting of decrements in performance of learned tasks were observed in pigeons which received a single injection of parathion (i.m., 0.56 mg/kg) or which received injections of 0.3 mg/kg/day for 3 weeks (McMillan, 1982). Monkeys, however, did not show any effects on learned behavioral tasks at oral dosages of parathion (0.05 or 0.14 mg/kg/day for 18 weeks) which produced decreases in plasma and RBC ChE (Hopper, 1977).

c. Developmental and Reproductive Toxicity

Parathion has been shown to produce malformations in avian species, including quail, duck and chicken (Bartalits et al., 1980; Meiniel, 1976; Meiniel, 1977; Proctor et al., 1976); however, terata have not been observed in mammalian test species. In two studies on file at the California Department of Food and Agriculture, no adverse fetal effects were observed at exposures that were not toxic to the mother. In one study (Schroeder, 1983a), rats were treated with 0, 0.25, 1.0 or 1.5 mg/kg/day (p.o.) on days 6-19 of gestation. Parathion was not teratogenic at the highest dose (1.5 mg/kg), although it did produce maternal toxicity (decreased survival, decreased body weights). The maternal NOEL was 1 mg/kg/day. In the other study (Schroeder, 1983b), female rabbits were

treated with 0, 1, 4, or 16 mg/kg/day (p.o.) on days 7-19 of gestation. Again, the highest dose (16 mg/kg) was not teratogenic. The maternal NOEL was 1 mg/kg.

Kimbrough and Gaines (1968) did not observe an increase in malformations when rats were injected intraperitoneally with either 3.0 or 3.5 mg/kg of parathion on day 11 of gestation, although these doses produced a significant increase in fetal resorptions. Toxicity to the dams was not assessed. Fetotoxicity (increased resorptions) was also observed in mice exposed via intraperitoneal injections to 10, 11, or 12 mg/kg/day on days 8, 9, and 10 or days 8, 10, 11, or i.p. injections of 12 mg/kg/day on days 12, 13, and 14 (Harbison, 1975). No resorptions were observed at a dose of 4 mg/kg/day in this study. Pups from dams treated with parathion from day 2 of gestation through day 15 of lactation (1.0 mg/kg/day, p.o.) showed effects on cardiac function on day 24 (Deskin et al., 1979); however, these effects were not observed under similar exposure protocols in a different strain of rats (Deskin et al., 1978).

No adverse reproductive effects were reported in a two generation reproductive study (Daly, 1982). In this study, male and female rats were fed diets containing 0, 0.5, 5, or 25 ppm of parathion. The only adverse effect reported was a decrease in body weights in the 25 ppm group. Clegg (1979) presented data from an unpublished report on a three generation reproductive study in a review article. In this study male and female rats were fed diets of 0, 10 or 30 ppm parathion and a decrease in survival to weaning of the F_1 offspring was seen in the 30 ppm group. Since details of the study were not included, the study is difficult to interpret.

Several studies have indicated that when parathion is incubated in vitro with liver or prostate preparations, testosterone metabolism is inhibited (Kuntzman et al., 1966; Donovan et al., 1978; Schein et al, 1977; Thomas et al., 1978). These effects, however, have not been reproduced following in vivo exposures of up to 5.2 mg/kg for 10 days in mice (Thomas and Schein, 1974; Thomas et al., 1977; Thomas, 1978). Additionally, changes in prostate weights (a sensitive indicator of testosterone imbalance) were not observed in these studies. Endocrine dysfunction in female rats was assessed by changes in estrus cycles, gonadotropins, and pituitary, ovary, and uterus weights following exposure to parathion at 0.114 mg/kg (p.o.) for 16 days (Bentue-Ferrer et al., 1981). Decreased uterine weights were the only changes observed.

d. Immunotoxicity

While very few studies are available on the immunotoxicity of parathion, those which were reviewed reported significant effects on the immune system at high doses. Casale and coworkers (1984) found an immunosuppression of primary IgM response in male mice treated with 16 mg/kg (p.o.) of parathion. No suppression was observed at 4 mg/kg. Male hamsters had a depression of both cellular and humoral immune responses following a single dose of parathion (p.o.) at 50% of the LD_{50} (exact dose was not stated; Dandliker et al., 1980). Finally, female mice demonstrated a decreased humoral response with a single dose by gavage at the LD_{50} or with 8 daily doses at the 0.1 LD_{50} (exact doses were not given; Wiltrout et al., 1978). While these studies do demonstrate effects on the immune

system, the effects were at doses which produced general toxicity. Selective immunotoxicity has not been observed.

e. Chronic Toxicity

Toxicity was assessed in both the dog and the rat in chronic feeding studies submitted to the California Department of Food and Agriculture. Male and female dogs (8/sex/group) were fed parathion at 0, 0.01, 0.03, or 0.1 mg/kg/day for one year (Ahmed, 1981). Blood chemistry, hematology, cholinesterase inhibition and clinical symptoms were monitored throughout the exposure period. Organ weights and histopathology were assessed at termination. Depression of cholinesterase activity was the only adverse effect reported in all of the treatment groups. RBC, plasma, and brain ChE's were depressed at 0.03 and 0.1 mg/kg/day in both sexes (>30% inhibition for all parameters). The cholinesterase values in the 0.01 mg/kg group were slightly depressed for both males and females, but the inhibition was not biologically significant.

Male and female rats (60/sex/group) were fed diets containing 0, 0.5, 5 or 50 ppm of parathion for two years (Daly, 1984). At the end of the study, plasma ChE and brain AChE were inhibited in both high-dose males and females with all ChE activities less than 20% of control; however, RBC AChE was not significantly depressed. Brain and RBC AChE's were not inhibited in the low and mid-dose groups. Plasma ChE was lowered in the mid-dose males and females (62 and 81% of control, respectively), although these values were not significantly different from controls. Plasma ChE was not depressed in the low-dose males and females.

Retinopathies described as uni- and bilateral retinal degeneration or atrophy were reported in the high-dose females. Additionally, a slight increase in other ocular effects (corneal scarring and posterior subcapsular cataracts) observed by direct ophthalmic examination were noted in both males and females in the high-dose group at 24 months. These effects were not present at 3 or 12 months.

Peripheral neuropathies were also reported in this study. High-dose females exhibited tremors during the first 3 months and an abnormal gait by the end of the experiment. Teased nerve fiber preparations showed significant increases in numbers of demyelinated lengths, fibers with myelin corrugations, and fewer normal fibers in high-dose rats of both sexes. Sciatic nerve lesions, consisting of myelin sheath degeneration, loss of myelinated fibers, Schwann cell proliferation, and the presence of cholesterol clefts, were also observed in high-dose males. Furthermore, morphometric studies in these males revealed the area of nerve occupied by myelinated fibers was decreased, and the internodal lengths were shortened. Low- and mid-dose males and low-, mid-, and high-dose females did not exhibit statistically significant changes. Oncogenic effects were also assessed in this study and will be reviewed in the oncogenicity section.

In a separate study, male and female rats were fed 0, 2, 8, or 32 ppm of parathion for 2 years (Eiben, 1986). Cholinesterase inhibition, ocular and sciatic nerve effects were assessed. Brain AChE was inhibited in males and females only at 32 ppm (39 and 23 % of control). RBC AChE activities were 88%, 73% and 63% for the low-, mid- and high-dose females; although, RBC AChE values were above 80% of control for males in all dose groups.

Plasma ChE activities were less than 70% of control for both sexes in the mid- and high-dose groups, but they were not depressed in the low-dose groups. Ophthalmic exams of pupil reflex, cornea, lens and fundus of retina did not indicate a treatment effect; however, the amplitudes of an electroretinogram in the 8 and 32 ppm females were significantly depressed. Microscopic ocular lesions were not observed in either sex at any dose level. Finally, histological evaluations of the sciatic nerves did not reveal parathion-induced lesions.

5. Mutagenicity and Oncogenicity

a. Mutagenicity

The mutagenic potential of parathion has been investigated in a number of test systems. The results of these studies are presented in Tables 14 - 16.

Most assays for gene mutations (Table 14) were negative; however, conflicting results were reported for *Salmonella* TA 1537 in a well conducted study (Haworth, 1983). These results may be due to different carrier solvents (95% EtOH or DMSO) used in the experiments. It should also be noted that concentrations used in the Haworth study covered a much broader range and were considerably higher than the other studies reported, which may account for the effects seen in this study and not others. In addition, a weak mutagenic response for paraoxon was reported for *Salmonella* TA98 and TA1538 without activation (Quinto et al., 1981). This study was not included in Table 14 since it was reported as an abstract and

TABLE 14

ETHYL PARATHION GENE MUTATION

Test System	Strain	Dose	Activation	Results	Reference	COMMENTS
S. typhimurium	TA 98	≤ 1.35 um/plate	+ (r + m)	neg	Bartsch 1980	Assays in triplicate,
	TA 100	≤ 1.35 um/plate	"	neg	"	Metabolic activation only.
S. typhimurium	TA 100	0.5-50 ug/plate	+, -	neg	Breau 1985	3 observations/experiment.
	TA 100	500 ug/plate	+	pos	"	No statistical analyses.
	TA 98	0.5-50 ug/plate	+, -	neg	"	Doubling of revertant colonies for positive result. S-9 system not specified.
S. typhimurium	TA 98	1 umol/plate	+ (m), -	neg	Nishimura 1982	No statistical analyses.
	TA 100	1 umol/plate	+ (m), -	neg		
S. typhimurium	TA 100	1, 5, 10, 50, 100, 500, 1000 ug/plate	+ (m), -	neg	Simmon 1977	3 replicates. No statistical analyses.
	TA 1535	1, 5, 10, 50, 100, 500, 1000 ug/plate	+ (m), -	neg	"	
	TA 1537	"	+ (m), -	neg	"	
	TA 1538	"	+ (m), -	neg	"	

TABLE 14, cont.

Test System	Strain	Dose	Activation	Results	Reference	Comments
S. typhimurium	TA 98	100, 333, 1000, 3333, 10,000 ug/plate	+ (r, h)	neg	Haworth 1983	3 observations/experiment, criteria for positive were subjective, based on increased revertants (not necessarily doubling) & dose response. Observations were later statistically confirmed by procedure of Margolin Two independent labs reported results.
	TA 100	100, 333, 1000, 3333, 10,000 ug/plate	+ (r, h), -	neg	"	Two highest doses precipitated in some experiments.
	TA 1535	"	+ (r, h), -	neg	"	
	TA 1537	"	+ (r, h), -	neg	"	Results from LAB #1, 95% EtOH originally reported as equivocal, later revised to negative.
	TA 1537	"	+ (r, h)	neg	"	Results from Lab #2, DMSO.
	TA 1537	0, 100, 333, 1000, 3333, 5000, 10,000 ug/plate	-	pos	"	Results from Lab #2, DMSO, 3 replicate experiments.
E. coli	WP2	1-1000 ug/plate	+ (m), -	neg	Simmon 1977	Reverse mutation to tryptophan independence, 3 replicates, no statistics.

TABLE 14, cont.

Test System	Strain	Dose	Activation	Results	Reference	Comments
Schizosaccharamyces pombe	SP-198	10 - 206 mM (parathion)	+ (m), -	neg	Gilot-Dehalle 1983	Forward mutation, ade 6-60/rad, 10-198/h$^-$.
		0.3 - 12 mM (paraoxon)	+ (m)	neg		
			-	pos		Approx. 20% increase at high dose only, marginal dose response, no statistics.
Drosophila		0.25-0.5 ppm feeding solution		neg	Waters 1980	Because of toxicity, higher doses were not tested.

r = rat; m = mouse; h = hamster

TABLE 15

PRIMARY DNA DAMAGE

Test System	Strain	Dose	Activation	Results	Reference	Comments
E. coli	W3110 p3478	1 mg/disc	-	neg	Simmon 1977	DNA polymerase (polA) deficient and proficient strains, assayed diameter of zone of inhibition. No difference between strains Assay performed in triplicate.
B. subtilis	H17/M45	1 mg/disc	-	neg	Simmon 1977	Proficient and deficient strains for DNA repair. No differences between strains in zones of inhibition. Assay performed in triplicate.
S. cerevisiae	D3	5 mg/ml	-, + (m)	neg	Simmon 1977	Results of 2 experiments. Percentage of survivors not different from negative control.

m = mouse, r = rat

TABLE 15 (cont.)

PRIMARY DNA DAMAGE

Test System	Strain	Dose	Activation	Results	Reference	Comments
Unscheduled DNA Synthesis (UDS)	WI-38	10^{-7} to 10^{-3}M	-	pos	Simmon 1977	Human diploid fibroblasts analyzed by ANOVA or Kruskal-Wallis non-parametric ANOVA, $p \leq .01$.
	"	"	+ (m)	neg		No dose response was observed in positive results.
Sister Chromatid Exchange (SCE)	Human Lymphoid LAZ-007	.02 - 20 ug/ml	-	pos	Sobti 1982	Dose related increase in SCE's, 3 replicates, analyzed by t-tests, $p \leq .01$
"	"	20 ug/ml	+ (r)	pos	"	Only dose treated w/ S-9.
SCE	Chinese Hamster Ovary (CHO)	0.03, 0.1 mM (parathion)	-	neg	Nishio 1981	Duncan's multiple range tests $p \leq .01$. 40 cells/sample, no replicate.
"	"	0.3, 1.0 mM (parathion)	-	pos	"	$p \leq .01$
"	"	0.03 mM (paraoxon)	-	neg	"	
"	"	0.1, 0.3 mM (paraoxon)	-	pos	"	$p \leq .01$

m = mouse; r = rat.

no details of the experimental methodology were available. Another positive response for paraoxon was observed in a forward mutation assay utilizing *Schizosaccharomyces pombe* (Gilot-Dehalle et al., 1983).

Assays for primary DNA damage (Table 15) presented the strongest evidence for genotoxicity of parathion. Positive findings were reported for unscheduled DNA systhesis (UDS) in human cells (WI38) without activation (Simmon et al., 1977), as well as increased incidences of sister chromatid exchange (SCE) in both human (LAZ-007) and hamster (CHO) cell lines (Nishio and Uyeki, 1981; Sobti et al., 1982). Additionally, paraoxon increased the number of SCE's in CHO cells without activation (Nishio and Uyeki, 1981). Conflicting studies on the ability of ^{14}C-parathion to bind to DNA have been reported. Murakami and Fukami (1980) found no DNA binding of ^{14}C-parathion in human embryonic lung cells, while Decloitre (1978) observed DNA binding to rat liver DNA, both in vitro and in vivo.

Finally, no chromosomal aberrations (Table 16) were detected from exposure to parathion or paraoxon when assayed by the dominant lethal test in male mice, nor by in vivo cytogenetic analyses of bone marrow cells, spermatogonia, and spermatocytes (Degraeve and Moutschen, 1984; Degraeve et al., 1984; Simmon et al., 1977). No data are available on the in vivo mutagenic potential of parathion in humans.

The overall assessment of parathion suggests that it may have genotoxic potential. Positive effects were observed in vitro in one strain of *Salomonella* and in several mammalian systems. Negative results, however, were reported for most in vitro assays utilizing microorganisms and for in vivo assays in mice.

TABLE 16

CHROMOSOME DAMAGE

Study Type	Species	Dose/Route	Results	Reference	Comments
Dominant Lethal	male mice Q strain	single i.p. injection 10 mg/kg 5 males/dose (parathion)	negative for pre- & postimplantation losses	DeGraeve and Moutschen 1984	Males were mated w/ 4 females per week for 7 weeks. Pre- and postimplantation losses analyzed by X^2.
Dominant Lethal	male mice Q strain	single i.p. injection 0.3 mg/kg 5 males/group (paraoxon)	negative for pre- & postimplantation losses	DeGraeve and Moutschen 1984	Males were mated w/ 4 females per week for 7 weeks. Pre- and postimplantation losses analyzed by X^2.
Dominant Lethal	male mice ICR/SIM	62.5, 125, 250 mg/kg/day (dietary) or approx. 0.44, 0.88, or 1.75 mg/kg b.w./day for 7 weeks	negative for post-implantation loss	Simmon 1977	Males were mated w/ 2 females per week for 8 weeks. Preimplantation losses determined. Data analyzed by t-test and chi-square test.

TABLE 16 (cont.)

CHROMOSOME DAMAGE

Study Type	Species	Dose/Route	Results	Reference	Comments
In vivo cytogenetics Bone Marrow and Spematogonia	male mice Q strain	single i.p. injection 10 mg/kg (parathion)	negative	DeGraeve and Moutschen 1984	At 12, 24, & 36 hr post injection, 4 males/group sacrificed at each timepoint. Chromosome breaks, exchanges and gaps were determined. Approx. 100 bone marrow metaphases/ animal, and 50-80 spermatogonial metaphases/animal, were analyzed.
"	"	single i.p. injection 0.3 mg/kg (paraoxon)	negative	"	"
In vivo cytogenetics spermatocytes	male mice Q strain	single i.p. injection 10 mg/kg parathion)	negative	DeGraeve et al., 1984	After 10 day recovery period, 2 males per day through day 15 were killed. 500 spermatocytes/male were analyzed. Chromosome aberrations (gaps, breaks, exchanges) were analyzed by X^2.
"	"	single i.p. injection 0.3 mg/kg (paraoxon)	negative	"	"

b. Oncogenicity

Parathion has been assessed for oncogenicity in several studies; however, a definitive conclusion as to the carcinogenic potential of this pesticide cannot be made at this time. EPA has established an interim classification for parathion as a Group C carcinogen (possible human carcinogen).

In a National Cancer Institute (NCI) study, male and female B6C3f1 mice (50/sex/group) were fed diets containing parathion at concentrations of 80 or 160 ppm. No treatment related oncogenic effects were observed (NCI, 1979). There were several problems with this study, however, which made the results difficult to interpret. First, there were only 10 concurrent controls/sex, although a large pooled control group was also used in the analyses. Second, the low-dose males were exposed for 71 weeks and the high-dose males for 62 weeks instead of the currently accepted 80-week protocol.

NCI also sponsored a feeding study in Osborne-Mendel rats (NCI, 1979). Male rats were exposed to 0, 32, or 63 ppm TWA (time weighted average) and female rats were exposed to 0, 23, or 48 ppm TWA (50/sex/group). Length of exposure (80 weeks instead of the currently accepted 110 weeks) and a small concurrent matched control group (10/sex) were also problems with this study. Increases in tumor rates were observed in low- and high-dose males and in high-dose females for adrenal cortical tumors (adenomas and carcinomas) using either the pooled (n=90) or matched (n=10) controls (Table 17). Adenomas were the principal lesions contributing to the significance of the combined tumors (adenomas: 9/46 high dose males and

TABLE 17

NCI CANCER BIOASSAY IN OSBORNE-MENDEL RAT

Tumor Type	Sex	Matched Control	Pooled Control	Low Dose	High Dose
Adrenal cortical[1] adenomas and carcinomas	Male	0/9	3/80	7/49	11/46
	Female	1/10	4/78	6/47	13/42
Pancreatic Islet[2] cell carcinoma	Male	0/9	0/79	1/49	3/46
Thyroid follicular[3] cell adenomas	Male	3/10	5/76	2/46	8/43

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1. Cochran-Armitage test for trend:
   males $p < .001$ for pooled controls
   males $p = 0.048$ for matched controls

   females $p < .001$ for pooled controls
   females $p = 0.028$ for matched controls

   Fisher Exact Test:
   males high dose vs. pooled controls $p < .001$
   females high vs. pooled controls $p < .001$

2. Cochran-Armitage test for trend:
   males $p = .024$ for pooled controls.
   Fisher exact test not significant.

3. Cochran-Armitage test for trend:
   males $p = .037$ for pooled controls.
   Fisher exact test not significant.

11/42 high dose females). Additionally, marginal responses in the form of significant trends for thyroid follicular cell adenoma and pancreatic cell carcinomas were observed in males when compared with pooled controls, but not with concurrent matched controls.

In a separate rat study, male and female Sprague-Dawley rats (60/sex/group) were fed diets containing 0, 0.5, 5 or 50 ppm of parathion for 2 years (Daly, 1984) (see description in Chronic Toxicity section). The initial evaluation indicated a significant increase in thyroid follicular cell adenomas in the high-dose (50 ppm) males compared to controls (5/58 or 9% vs 0/60 or 0%). However, reanalyses of the data revealed one less high-dose tumor and the revised incidence (6.8%) was reported to be within historical control values from this laboratory (0 - 8%) based on observations in 1,163 male Sprague-Dawley rats from 14 studies. No follicular cell carcinomas were seen in any treatment group. The percentages of thyroid C-cell adenomas and carcinomas were comparable among the groups. Finally, the occurrence rates of adrenal cortical adenomas and carcinomas were high in all groups, and no treatment related effects were apparent.

B. Risk Characterization

Parathion is extremely toxic and has been designated as a Category I pesticide by EPA. In addition, EPA has assigned parathion an interim classification as a Group C carcinogen (possible human carcinogen), and it has required additional studies to determine the oncogenic potential of parathion. This section has been divided into oncogenic and nononcogenic risks and, because of the extreme toxicity of this compound, acute, subchronic and chronic risks will be addressed in the nononcogenic effects section.

1. Nononcogenic Effects

In determining the risks of exposure to parathion, two assumptions were made. First, 100% absorption following inhalation was assumed. This was based on the similarity of the i.v. LD_{50} and the inhalation LC_{50} for the rat (Table 11), as well as the nearly complete absorption following endotracheal administration in the rat (Nye and Dorough, 1976). Additionally, there were some indications in human studies that parathion is readily absorbed by the lungs (Durham et al., 1972; Hartwell et al., 1964, 1965). While these are not definitive studies on lung absorption, in lieu of other data, complete absorption will be assumed. The second assumption is that the threshold at which the inhibition of plasma or RBC

cholinesterase becomes biologically significant is 30% (i.e. 70% of control values). No clinical signs have been observed at this level of depression in humans or animals. Studies have indicated that there is considerable variability in cholinesterase activities and that one cannot assume an effect has occurred until the plasma and/or RBC values are less than 70% of normal (Callaway, et al., 1951; Gage, 1967). In general, greater weight will be placed on RBC and tissue (particularly brain) acetylcholinesterase depression than plasma cholinesterase depression, since plasma cholinesterase assays are not specific for acetylcholinesterase.

Species respiratory volumes, interspecies conversion factors, margin of safety and other calculations used in the following sections are presented in Appendix 1.

a. Risks Following Acute Exposures

Parathion is a Category I pesticide, which is the highest ranking for acute toxicity. Poisonings from parathion exposures have occurred among all categories of agricultural workers (EPA, 1986). While data exist for lethal doses and for doses which substantially inhibit cholinesterase in humans, no data are available for low-dose exposures.

The lowest NOEL for inhibition of RBC AChE is 1.21 mg/m^3 in the rat (4 hour exposure) (NIOSH, 1976; Owens, 1977). Using this NOEL and multiplying by a species conversion factor of 3.7 for adults and 2.1 for children to correct for the human's respiratory volume, the adult equivalent air concentration is 4.48 mg/m^3 and the equivalent for the child is 2.5 mg/m^3

for four hour exposures (Table 18). The highest short term or acute exposures were reported to be 34 ug/m^3 (15 minute sample), 40 yards off site during an application and 3.09 ug/m^3 at the same site for 0-2 hours post application (Table 5c). While the actual NOEL for these exposure periods (up to two hours) may be greater than the NOEL for estimated from the four hour exposure, we did not feel confident extrapolating to these shorter periods using the current data base. Hence, the margins of safety are based on the human equivalent concentrations of 4.48 mg/m^3 (adult) and 2.5 mg/m^3 (child). The MOS's for exposure to 34 ug/m^3 are 100 and 74 for the adult and child and the MOS's for exposure to 3.09 ug/m^3 are 1550 and 800 for the adult and child.

The extrapolated values for 24 hour exposure from these NOEL's (4.48 mg/m^3, adult, and 2.5 mg/m^3, child) are 0.75 mg/m^3 and 0.42 mg/m^3 for the adult and child, respectively. The highest 24 hour value for ambient exposure was 1.423 ug/m^3 measured at Parlier (Tables 6 and 7). Using the NOEL's extrapolated to a 24 hour exposure period, the MOS's are estimated to be 500 for the adult and and 300 for the child.

b. Risks of Subchronic Exposures

Cholinesterase inhibition was the only adverse effect reported in the subchronic studies. The inhalation route of exposure (7 hr/day, 5 days/week, 6 weeks) produced the lowest NOELs in both the rat and the dog (NIOSH, 1976; Owens, 1977). The NOEL for the rat is 0.01 mg/m^3. The estimated equitoxic concentration for an adult human is 0.011 mg/m^3 and for a child is 0.006 mg/m^3, after adjusting for interspecies differences in respiratory rates (conversion factor of 3.7 and 2.1) and correcting for 24

hour exposures. The MOS for cholinesterase inhibition from the rat data is 65 for adults and 35 for children when the mean exposure value (0.170 ug/m^3) from the northern San Joaquin Valley is used (Tables 6 and 7). This area was selected because it had the highest set of ambient exposures. The NOEL for cholinesterase inhibition from the dog data is 0.01 mg/m^3 which converts to a human equivalent concentration of 0.004 mg/m^3 (adult) and 0.002 mg/m^3 (child) based on 24 hour exposure and an interspecies conversion factor of 1.5 and 0.8. This provides a MOS of 24 and 12 (adult and child, respectively) for cholinesterase inhibition.

Several studies performed on volunteers and workers indicated that the oral NOEL for RBC AChE inhibition is 0.05 mg/kg/day over 3 and 6 week exposure periods (Edson, 1964; Rider et al., 1958). The conversion to air concentration is 0.19 mg/m^3 for an adult and 0.11 mg/m^3 for a child, with a MOS of 1000 and 600 based on an exposure of 0.170 ug/m^3.

The range of risks from subchronic studies on parathion is quite large. All three studies were presented because none of them were definitive studies. While it is preferable to determine risks from human data, the human study utilized oral exposure, therefore requiring an extrapolation to determine an equivalent dosage via inhalation. Additionally, parathion undergoes significant first pass metabolism, and hence, the extrapolated inhalation NOEL from oral data may underestimate the risk. On the other hand, while the rat and dog studies were inhalation studies, they required interspecies conversions. Moreover, the assumption that these studies were whole body exposures presents the possibility of additional exposure via dermal and oral absorption, which could overestimate the risk.

c. Risks of Chronic Exposure

The most serious adverse effects associated with chronic dietary exposures of parathion were the retinopathies and neuropathies observed in rats (Daly, 1984). The NOEL for these effects is 5 ppm or 0.25 mg/kg/day, which is also the NOEL for RBC and brain AChE inhibitions. While plasma ChE was lowered in the males at this dose, the lack of depression in RBC and brain AChE's indicated that this is the most reasonable threshold dose. The NOEL from the second rat dietary study is 2 ppm (Eiben, 1986), based on RBC AChE depression and ophthalmic effects. This NOEL will be used for risk assessment since it is lower than the NOEL from the Daly study and it should be protective of the adverse effects identified in that study. This feed concentration (2 ppm) converts to 0.1 mg/kg/day which is equivalent to 0.1 mg/m^3 (based on a 24 hour exposure). The human equivalent dose is 0.37 mg/m^3 (adult) and 0.21 mg/m^3 (child), which provides a MOS of 2200 and 1200 for adults and children for cholinesterase inhibition and ophthalmic effects using the highest mean exposures (0.170 ug/m^3).

The dog was the most sensitive species tested for chronic effects, although the only adverse effect reported was cholinesterase depression (Ahmed, 1981). The NOEL from this study is 0.01 mg/kg/day. The human equivalent air concentration for the NOEL is 0.039 mg/m^3 for the adult and 0.02 for the child, based on the respiratory volume for the dog (0.39 $m^3/kg/24$ hr) and a species conversion factor of 1.5 and 0.8. The MOS's for cholinesterase inhibition are 200 and 100 for the adult and child, respectively, using 0.170 ug/m^3 as the exposure estimate.

2. Oncogenic Effects

Parathion has been categorized as a Group C carcinogen (possible human with limited evidence of carcinogenicity in animals in the absence of human data) by EPA. The Agency based this conclusion on the NCI mouse and rat studies as well as the the rat study by Daly (NCI, 1979; Daly, 1984). The International Agency for Research on Cancer (IARC) has reviewed the data from the NCI mouse and rat studies, but not the Daly rat study, and concluded that there is inadequate evidence to evaluate the carcinogenic potential of parathion (IARC, 1982).

The Health Assessment Group in the Medical Toxicology Branch of California Department of Food and Agriculture has determined that, at the present time, only limited evidence exists for the carcinogenicity of parathion in animals, and that there are insufficient data with which to conduct a quantitative risk assessment. This decision was based on the following evidence: the carcinogenic response was observed in one strain of one species (Osborne-Mendel rat); the increase in tumor occurence rates was in adrenal cortical tumors, which have a high background rate; there were design flaws in this study; and, other studies were negative (one in Sragues-Dawley rats and one in B6C3f1 mice). In addition, definitive conclusions about the genotoxic potential of parathion could not be made. As additional studies become available, the oncogenic potential of parathion will be reevaluated.

3. Conclusion

A summary of the risks associated with reported parathion exposure values is presented in Table 18 and the predicted exposure values for 10-fold and 100-fold margins of safety are presented in Table 19. The margins of safety (MOS) range from 12 to 1200 for a child and from 24 to 2200 for an adult depending on the route and duration of the exposure, and the species used for the assessment. All of the margins of safety were based on cholinesterase inhibition, and the smallest margins of safety were extrapolated from subchronic inhalation studies in dogs and rats. A ten-fold MOS for cholinesterase inhibition is generally considered adequate for an adult based on doses which produce a 30% inhibition (i.e. cholinesterase activity at 70% control). A 30% inhibition represents a biological threshold, and no functional, clinical, or pathological effects are associated with it. However, for infants and small children, a twenty-fold MOS is recommended. This value is based on studies which showed that plasma cholinesterase and RBC acetylcholinesterase activities in infants are normally significantly below adult levels (up to 50%) for approximately the first 6 months of life (Karlsen et al., 1981; Kaplan et al., 1963; Neal and DuBois, 1965). Animal studies have indicated that LD_{50}'s for adult rats from parathion and other organophosphate pesticides are 2 to 5 times greater than LD_{50}'s for newborn and weanling rats (Harbison, 1974; Virgo, 1984). Other sensitive subpopulations, such as asthmatics, persons under treatment with β-blockers, and individuals being treated for neuromuscular

TABLE 18
SUMMARY OF RISKS

Effect[a]	Dose	Human Equivalent Dose Adult	Human Equivalent Dose Child	Exposure[d]	Margin of Safety Adult	Margin of Safety Child
Acute:						
NOEL, AChEI rat	1.21 mg/m^3 (4 hr)	4.48[b]	2.50[b]	34 ug/m^3 3.09 ug/m^3	100 1500	74 800
NOEL, AChEI rat	1.21 mg/m^3 (4 hr)	0.75[c]	0.42[c]	1.423 ug/m^3	500	300
Subchronic:						
NOEL, AChEI rat	0.01 mg/m^3 (7 hr)	0.011[c]	0.006[c]	0.170 ug/m^3	65	35
NOEL, AChEI dog	0.01 mg/m^3 (7 hr)	0.004[c]	0.002[c]	0.170 ug/m^3	24	12
NOEL, AChEI human, oral	0.05 mg/kg per day	0.19 [c]	0.11[c]	0.170 ug/m^3	1000	600
Chronic:						
NOEL, AChEI, ophthalmic effects-rat	2 ppm(diet) (0.10 mg/m^3)	0.37[c]	0.21[c]	0.170 ug/m^3	2200	1200
NOEL, AChEI dog	0.01 mg/kg/d (0.026 mg/m^3)	0.039[c]	0.02[c]	0.170 ug/m^3	200	100

a. NOEL = no observed effect level; AChEI = acetylcholinesterase inhibition.
b. mg/m^3/4 hours
c. mg/m^3/day
d. Exposure data from Tables 5c, 6 and 7.

TABLE 19
PREDICTED EXPOSURE VALUES FOR RANGE OF MARGINS OF SAFETY

	Margins of Safety			
	10		100	
Effect	Adult	Child	Adult	Child
Acute:				
AChEI, rat[a]	450 ug/m^3	250 ug/m^3	45 ug/m^3	25 ug/m^3
AChEI, rat[b]	75 ug/m^3	42 ug/m^3	8 ug/m^3	4 ug/m^3
Subchronic:				
AChEI, dog	0.4 ug/m^3	0.2 ug/m^3	0.04 ug/m^3	0.02 ug/m^3
AChEI, human[c]	19 ug/m^3	11 ug/m^3	2 ug/m^3	1 ug/m^3
Chronic:				
AChEI, dog[c]	4 ug/m^3	2 ug/m^3	0.4 ug/m^3	0.2 ug/m^3

a. Based on four hour exposure.
b. Based on 24 hour exposure.
c. Based on oral data.

disorders with anticholinesterase drugs, may also be at an increased risk from exposure to parathion (Taylor, 1985). Finally, concurrent exposure to other cholinesterase pesticides may produce additive or synergistic effects which could affect the estimated margins of safety.

In determining the margins of safety for parathion, a number of conservative assumptions were made. First, inhalation absorption was assumed to be 100% . Second, the single highest 24-hour exposure value was used for the MOS based on acute health effects data as well as exposure values obtained during and immediately following application at sites adjacent to the sprayed fields. Third, only the detectable (positive) exposure values were used for determining the mean 24-hour exposures and, then, the highest mean value was used. Finally, it was assumed that exposure would continue at the highest mean value throughout the exposure periods.

Exposure to parathion at the reported ambient air concentrations at sites remote from the area of application does not appear to pose a threat to human health as determined by the currently available data. Furthermore, the air concentrations of parathion measured during and immediately following application at sites adjacent to the field were not likely to produce adverse effects; however, accidental exposures at these sites, particularly from misapplication, could present potential problems related to acute health effects. The smallest margin of safety for cholinesterase inhibition was 12 for the child based on inhalation data obtained from a study in dogs. Although this value is below a MOS of 20, it is considered adequately protective. This conclusion was based on the

fact that conservative assumptions were used throughout the risk assessment, the MOS for acute effects (cholinesterase inhibition) in the most extreme case was approximately 75 for the child, and the MOS for cholinesterase inhibition for the child based on human data was 600. Furthermore, the current acceptable daily intake (ADI) for parathion is 0.005 mg/kg/day based on a NOEL in humans of 0.05 mg/kg/day with a 10-fold safety factor (EPA, 1986). The ADI converts to an equivalent concentration in the air of 0.011 mg/m^3 (assuming a child 24-hour respiratory volume of 0.46 m^3/kg). The highest mean exposure was 0.170 ug/m^3 which is equivalent to 1.5% of the ADI. The American Conference of Governmental Industrial Hygienists have set a TLV-TWA (threshold limit value- 8 hour time weighted average) at 0.1 mg/m^3, which is greater than 100-fold above the ambient exposures.

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APPENDIX I

CONVERSION FACTORS

Animal Species	Conversion Factor (dry food) 1 ppm in Food Equals in mg/kg/day	
Mouse	0.15	
Rat (young - 0.10 kg)	0.10	
(older - 0.40 kg)	0.05	
Guinea Pig	0.04	
Rabbit	0.03	
Monkey	0.05	(semi-solid)
Cat	0.05	(semi-solid)
Dog	0.03	
Man (70 kg)	0.03	(semi-solid)
Woman (55 kg)	0.03	(semi-solid)

Animal Species	Respiratory Volume[a] (m^3/kg/24hour)	Conversion Factors Adult	Child
Mouse	1.80	6.9	3.9
Rat	0.96	3.7	2.1
Guinea Pig	0.45	1.7	1.0
Rabbit	0.54	2.1	1.2
Rhesus Monkey	0.48	1.8	1.0
Cat	0.20	0.8	0.4
Dog	0.39	1.5	0.8
Adult (70 kg)	0.26 b	-	
Child (13 kg)	0.46 c	-	

a. Zielhuis and van der Kreek, 1979.
b. Based on a respiratory volume for light work of 11 m^3/10 hr and a resting respiratory volume of 7 m^3/14hr, for a 24 hour respiratory volume of 18 m^3.

c. Based on a respiratory volume for light activity of 3.5 m^3/8 hr and a resting respiratory volume of 2.5 m^3/16 hr, for a 24 respiratory volume of 6 m^3.

CALCULATIONS:

mg/kg to mg/m^3: mg/kg divided by m^3/kg = mg/m^3

mg/m^3 to mg/kg: mg/m^3 X m^3/kg = mg/kg

$$\text{Margin of safety (MOS)} = \frac{\text{NOEL or LOEL } (ug/m^3)}{\text{Observed ambient air concentrations } (ug/m^3)}$$

V. Department of Health Services Staff Review of the "Evaluation of Ethyl Parathion as a Toxic Air Contaminant - August 1987"

October 1, 1987

Department of Health Services Staff Review of the
"Evaluation of Ethyl Parathion as a Toxic Air Contaminant"
prepared by the Department of Food and Agriculture

In response to the request by the Department of Food and Agriculture (CDFA), the ethyl parathion document has been reviewed by staff of the Air Toxics and the Pesticides Units in the Department of Health Services (DHS). DHS staff agree that existing concentrations of parathion are unlikely to result in an increase in illness or mortality. However, as indicated below, certain aspects of the health assessment need to be addressed to clarify the potential hazards of the compound.

General Comments

In general, the document is a well-written report describing the hazards associated with use of ethyl parathion as an agricultural pesticide. Parathion is very hazardous because it is rapidly absorbed through the skin, the gastrointestinal tract and the lungs. It is metabolized to paraoxon in the liver. Paraoxon inhibits acetylcholinesterase (AChE) in red blood cells and in the nervous system.

Exposure to Parathion and Paraoxon

The report indicates that paraoxon is responsible for parathion's toxicity. It is also reported that the half-life for conversion of parathion to paraoxon in the air ranges from 2 to 131 minutes. However, only concentrations of ethyl parathion were included in the report, even though paraoxon was measured in some samples. In fact, paraoxon was measured on the days in which ethyl parathion levels were reportedly the greatest (Table 8A). It would appear that paraoxon levels should be included in the exposure evaluation. Since paraoxon is more toxic than parathion, a weighted exposure concentration could be calculated. This weighted value could then be used as the exposure estimate.

It is not clear why 24 hours was chosen for the sampling time period (Chapter III). A one or three-hour period would be more suitable for evaluating the potential for acute toxicity.

Reevaluation of Toxicity Data

The toxicity studies, in particular the inhalation studies, need to be more extensively evaluated by CDFA to determine which ones are acceptable for use in risk assessment (Tables 10, 11, 12). Inadequate studies should be discarded from the final risk assessment. The methods developed for exposing laboratory animals are simple for oral and dermal routes, but the quantitative administration of a pesticide aerosol or vapor is complex. In past years, investigators may have used unsatisfactory methods for determining the toxicity of an inhaled pesticide by contaminating the skin, allowing animal self-grooming and oral exposure. Inhalation toxicity data

gathered under these conditions should not be used in the risk assessment because the information may misrepresent the toxic potency of parathion.

Calculation of Absorbed Dose

Whenever possible the percent of dose absorbed by each species should be incorporated in the report's health effects analysis (pages 66 to 68). The administered air concentration may not accurately reflect the dose expected to be absorbed by humans if the animal species and humans have different lung absorption rates. CDFA staff should consult the study entitled "Inhalation uptake of selected chemical vapors at trace levels," performed by Dr. Raabe at UC Davis for the Biological Effects Research Section, California Air Resources Board (CARB Contract No. A3-132-33, May 1986).

Determining the Appropriate Species for Extrapolation to Man

The rat, a nose-breather, is considered to be a poor animal model for inhalation studies, because a large percentage of the administered dose (up to 90%) may be removed from the airstream by the nasal turbinates before the pesticide reaches the lung. Animals such as the dog and monkey are considered to be more acceptable animal models because they breath through their mouth and nose and their respiration rates are similar to man. Consequently, it may be more prudent to base the health risk assessment on data from the dog than the rat.

Incorporation of Available Human Data

DHS staff suggest that additional human data be incorporated into the risk assessment. The results of the human and dog uptake studies of Dr. Raabe may be used to estimate the dose of parathion likely to be retained by Californians living in agricultural areas. Resting male volunteers inhaled 7.0 to 8.3 liters of air per minute, while females inhaled 5.8 to 6.0 liters per minute. Respiration rate varied between 10 and 13 breaths per minute. If air contained 0.8 $\mu g/m^3$ of parathion, and if 50% of the parathion were retained in the lung, the dose rate for a 70 kg man at rest (8.0 liters/minute) would be 2.74 ng/kg/hr. On the basis of a human no-observed-effects level (NOEL) of 0.05 mg/kg/day or 2080 ng/kg/hr (Edson 1964, Rider et al. 1958), a margin of safety of 759 would be calculated for the highest daily air concentration. Lower concentrations in air would result in greater margins of safety. However, as stated below, using a larger respiratory volume to account for increased ventilation rates due to physical activity would decrease the margin of safety.

Definition of the Margin of Safety

The report initially defines the margin of safety (MOS) as the ratio of the no-effect level to the exposure level (page v and Appendix I). However, in the body of the report, MOS values are calculated for lethality endpoints. The MOS calculations should be restricted to comparisons of ambient levels to no-effect levels or estimates of no-effects levels.

Evaluation of the Reported Margins of Safety

CDFA should give greater guidance on the quality of the MOS range, which is reported to be from 30 to 2734. CDFA should provide more insight as to which value, 30 or 2734, is the best estimate for the MOS, or indicate that all values within that range are equally likely. A disturbing factor about the analysis is that the smallest MOS (30) was determined by a low-effect level and not a no-effect level. Thus, the range of MOS for chronic exposure has not been adequately defined.

The report discusses the toxicity in terms of acute, subchronic or chronic exposures. It would be more helpful if the report summarized the MOS in terms of the length of exposure. For example, according to Table 13, the MOS for an acute exposure is 923; the MOS for a subchronic exposure ranges from 39 to 1439; and the MOS for a chronic exposure ranges from 30 to 7122. This type of presentation quickly brings to mind that there is extensive overlap of the margins of safety for acute and chronic exposures; the reason for the overlap should be discussed.

The effect evaluated for the margin of safety represents a threshold response. Since ethyl parathion exposure also occurs by other routes, particularly the oral route, estimates should also be considered for simultaneous multipathway exposure in calculating the MOS.

Carcinogenicity of Parathion

Based on the evidence presented in the report (pages 63-65), there appears to be inadequate evidence for carcinogenicity of ethyl parathion. However, the US EPA has classified it as a possible human carcinogen. This apparent inconsistency should be clarified.

Considering Children in the Evaluation

The margin of safety for exposure of children to ethyl parathion should be estimated. This is particularly important since according to estimated lethal thresholds, children (LD_{lo} = 0.1 mg/kg, Table 10) are much more susceptible to parathion toxicity than the most sensitive animal species, the dog (LD_{lo} = 2.5 mg/kg, Table 13). Furthermore, children breathe more per unit weight than do adults.

Estimated Breathing Rates

The conversion factors used to estimate respiration rate and respiratory volume differ from those used by DHS. DHS staff suggest that for a 60 kg adult, 18 m^3/day should be used, instead of 15 m^3/day used in the report. For children, respiratory data are cited in Hawley et al. (1985. Risk Analysis 5:289-302); an estimate of 8.5 m^3/day appears to be suitable for a 13.2 kg child. This estimate would be equivalent to 0.64 m^3/kg/day, which is 2.5 times greater than the adult rate cited in Appendix 1.

Future Reports

Future reports evaluating the potential effects of organophosphate pesticides should probably consider their additive impact. Similar pesticides may be used concurrently with parathion. Since the organophosphates exert their toxicity in a similar manner (cholinesterase inhibition) their effects would be additive.

VI. The CDFA's Responses to Department of Health Services Comments on the "Evaluation of Ethyl Parathion as a Toxic Air Contaminant" - January 1988

January 19, 1988

Responses to Department of Health Services comments on the "Evaluation of Ethyl Parathion as a Toxic Air Contaminant"

1. Exposure to parathion and paraoxon

In response to the comment by DHS regarding exposure to parathion and paraoxon, we have included paraoxon levels in our exposure evaluation. We took all samples containing measured levels of paraoxon, converted those levels to parathion equivalent values, and added those values to the concentration of parathion found in the same samples. Data were not found which could be used to weight paraoxon relative to parathion levels in regard to their relative toxicities. Therefore, a simple summation of values was performed rather than a weighted exposure calculation. In the January 1988 draft, paraoxon values have been tabulated in Table 8B. The summed values have been inserted into the appropriate tables (Tables 6, 7, 8C).

In response to the comment questioning the use of 24-hour sampling periods, 3-hour samples were taken over selected time periods. However, the majority

of samples were over 24-hour periods in order to increase the time frame for the studies and decrease the number of samples to be analyzed.

2. Reevaluation of Toxicity Data

The criticism of methods for exposure in inhalation studies is valid. Nose-only exposure is the appropriate method for acute and subchronic study designs; however, nose-only exposure for chronic studies with sufficient hours of exposure (i.e. 6-7 hours/day) is unsuitable due to the excessive stress which would be placed on the animals. Henry and Kouri (1987)* reported that nose-only exposures of 2 hours/day produced decreased weight gain in sham-exposed control animals compared to unrestrained controls. While the use of data from a whole body exposure study may misrepresent the toxic potency of the compound, these data may still be preferable to the use of oral exposure data which would require a route-to-route extrapolation.

Three inhalation studies, conducted at the Edgewood Arsenal for NIOSH, were selected for risk assessment. It was determined that these studies were whole body exposures; however, we felt that they were adequate and, in lieu of any other inhalation data, we decided to incorporate them into the risk analyses.

* Henry C.J. and Kouri R.E. 1987. Specialized test article administration: nose-only exposure and intratracheal inoculation. In: Inhalation Toxicology

Research Methods, Applications, and Evaluations. Occupational Safety and Health Series No. 12, Alan L. King, ed. Marcel Dekker, Inc., New York, pp. 121-134.

3. Calculation of absorbed dose

The study by Dr. Raabe at UC Davis was reviewed by the Medical Toxicology staff. Adult female beagle dogs were exposed to low concentrations of one of six organic vapors, which included methyl bromide, chloroform, benzene, trichloroethylene, formaldehyde, and dimethylnitrosamine. The fractional systemic uptake of total vapor ranged from 39.5% to 54.4%. While we recognize that only a certain percentage of the aerosolized parathion would be absorbed by the lungs, we felt that the compounds used in the Raabe study were too dissimilar to parathion to be used for estimation of absorption. In lieu of more definitive information on the absorption of parathion, 100% absorption will be assumed.

4. Determining the appropriate species for extrapolation to man

The selection of studies for risk assessment is based upon many considerations such as the quality of the study, adverse effect, route of exposure, etc. The use of the most appropriate animal model is one of the

factors in this decision. Data obtained from two dog studies (one inhalation and one oral study) were used for the determination of risks.

5. Incorporation of available human data

The data from Edson (1964) and Rider et al. (1958) were used for the risk assessment. Absorption was assumed to be 100% based of the reasons explained in #3.

6. Definition of the margin of safety

The margins of safety based on lethality as endpoint were eliminated. The definition of margin of safety was correct.

7. Evaluation of the reported margins of safety

Upon reevaluation of the chronic dog study, the 0.01 mg/kg/day dosage was changed from a LOEL to a NOEL. This dose was originally designated as a LOEL because of the depression in brain AChE in the male dog (51% of control activity). This value, however, was not statistically significant due to the high variability in the control group, which stemmed from several excessively high values. Brain AChE in female dogs was not depressed (133%

of control). No other effects were noted, including histopathology, at this dose or at the higher doses (0.03 and 0.10 mg/kg/day).

Several studies were eliminated from the risk assessment which had very large margins of safety. These included acute lethal thresholds in the rat and dog and a one of two chronic dietary studies in the rat.

The risks were broken into categories based on acute, subchronic or chronic data and the concordant exposure values were used. In lieu of more definitive exposures values for year-round exposures, the estimates generated for the short term (subchronic) exposures were used for calculation of the risks associated with long term exposures. There was considerable variability both within and across these categories for the MOS estimates which was a function of both exposure data and health effects data used.

The margins of safety based on cholinesterase inhibition associated with subchronic or short term exposures had the widest range of values (16 to 1319). The lowest values were based on dog and rat inhalation studies, while the highest values were based on oral human exposures. We felt that despite the variability, all of these data needed to be considered in the risk assessment. The inhalation studies were included even with their design flaws because of the possibility of local effects of parathion on the lung, which may make this route particularly sensitive to parathion exposure. The human data were used since these were the only experimental

data available in humans, and because EPA and FAO/WHO used these data for the establishment of their ADI's.

The MOS's for the chronic studies range from 139 to 2569. While depression of acetylcholinesterase activity was the most sensitive endpoint, the NOEL for ophthalmic effects observed in a chronic rat feeding study were included because of current concern over these lesions. The MOS for these lesions were an order of magnitude above the MOS for cholinesterase inhibition in the dog in a chronic feeding study.

8. Carcinogenicity of parathion

The assessment of the oncogenic potential of parathion was based on the results of the three carcinogenesis assays reviewed and on the collective mutagenicity data. The weight of evidence indicated that there was only limited evidence of carcinogenicity and that a quantitative risk assessment would not be appropriate at this time. This decision was based on the following evidence: the carcinogenic response was observed in one strain of one species (Osborne-Mendel rat); the increase in tumor occurrence rates was in adrenal cortical tumors, which have a high background rate; there were design flaws in this study; and two other studies were negative (one in a different strain of rat and one in mice). Additionally, definitive conclusions about the mutagenic potential of parathion could not be made.

A copy of the Risk Assessment Guidelines developed at the Department of Food and Agriculture has been included.

While EPA designated parathion as a Class C carcinogen (possible human carcinogen) in the Guidance for the Reregistration of Pesticide Products Containing Parathion, 1986 based on the same three studies, they did not conduct a quantitative risk assessment for parathion.

9. Considering children in the evaluation

Risks for children were calculated and added to the risk assessment section.

10. Estimated breathing rates

Breathing rates were reviewed and brought more in line with DHS and EPA values (see Appendix).

VII. Public Comments to the "Evaluation of Ethyl Parathion as a Toxic Air Contaminant - December 1987"

BUTTE COUNTY MOSQUITO ABATEMENT DISTRICT

DISTRICT OFFICE AT
N. E. CORNER OF OROVILLE AIRPORT
ON LARKIN ROAD
PHONE (916) 533-6038
342-7350

5117 LARKIN ROAD
OROVILLE, CALIFORNIA 95965

WILLIAM E. HAZELTINE, PH.D.
MANAGER - ENVIRONMENTALIST

December 17, 1987

Mr. Ronald Oshima
CDFA, Room A 149
1220 N Street
Sacramento, CA 95814

Dear Mr. Oshima:

Thank you for the Draft Report on Parathion as a Potential Air Contaminant. You have done a good job in reviewing the hazards of Parathion to people.

The only suggestion we would make is to expand the user group reference to include public health, along with agriculture. While the volume used for mosquito control is small, it is not insignificant in terms of health protection, and any attempt to restrict the use of Parathion, based on a health risk basis, should also take into account the health benefits as well as crop production. We use Parathion to control the vectors of encephalitis and malaria, during the mid-summer period. In addition, when used for rice production, farmer applied Parathion also controls early season mosquitoes as well as tadpole shrimp.

I assume the statutory mandate under which your study was done did not require or even allow benefit considerations, and therefore only risks were addressed. I would personally like to see this imbalance at least mentioned, but perhaps political realities will not allow such comment. CDFA needs to continue to be a strong advocate of all balanced pesticide uses, as they were in times past.

Sincerely,

William E. Hazeltine, Ph.D., R.P.E.
Manager/Environmentalist

WEH/db
cc: Don Womeldorf, DHS

South Coast
AIR QUALITY MANAGEMENT DISTRICT
9150 FLAIR DRIVE, EL MONTE, CA 91731 (818) 572-6200

December 30, 1987

Department of Food and Agriculture
Environmental Monitoring and
Pest Management, Room A-149
1220 N Street
Sacramento, CA 95814

Attention: Kimi Klein

The South Coast Air Quality Management District has reviewed the draft document "Evaluation of Ethyl Parathion as a Toxic Air Contaminant" and wishes to submit the enclosed comments for your consideration. If you have any questions concerning these comments please contact Mark Saperstein at (818) 572-2118.

Very truly yours,

Jo Anne H. Aplet
Director of Planning

MS:ak

Enclosure

December 30, 1987

SOUTH COAST AIR QUALITY MANAGEMENT DISTRICT

COMMENTS ON THE DRAFT EVALUATION OF ETHYL PARATHION AS A TOXIC AIR CONTAMINANT

1) Species Specificity of Pesticides

Residents that may be exposed to pesticides from aerial application may wish to know why these compounds are lethal to insect pests but cause no apparent harm to humans at similar concentrations. It would be useful to include a section briefly describing the species specificity of ethyl parathion. This would benefit individuals who consult this document because of concerns about potential adverse health effects.

2) Maximum Ambient Concentration and Maximum Exposed Individuals

The maximum concentration which occurred in a 24 hour sample was 0.871 ug/m^3. However, it is not clear if this is the highest concentration of parathion which could result from pesticide use since the sampling program was not designed to coincide with specific (i.e. same day) periods of pesticide application. The maximum concentrations which could result from pesticide use at a nearby residential receptor should be estimated (perhaps through dispersion modeling) and this concentration should be compared to short-term ambient concentrations which would be considered acceptable.

3) Estimation of a Threshold Concentration for Adverse Health Effects

It is concluded in the document that no adverse health effects would be expected at concentrations which have been measured in California. However, one goal of the document is to provide "an estimate of the levels of exposure in air which may cause or contribute to adverse health effects". The document does not clearly specify a concentration which should be considered a threshold for adverse health effects. Should it be assumed that the Department of Food and Agriculture agrees with the FAO/WHO acceptable daily intake (ADI) level of 0.005 mg/kg/day (0.019 mg/m^3) as cited on page 91 of the document? The specification of a threshold value or ADI would be useful with respect to future evaluations of ambient concentration data for this compound.

4) Decision Criteria for Classifying Carcinogens

In performing this evaluation (and in future evaluations of toxic air contaminants) the Department of Food and Agriculture must decide what "weight of evidence" will be considered sufficient to classify a pesticide as a carcinogen. It is stated in the document;

> "The Health Assessment Group in the Medical Toxicology Branch of the California Department of Food and Agriculture has determined that, at the present time, only limited evidence exists for the carcinogenicity of parathion in animals, and that there are insufficient data with which to conduct a quantitative risk assessment."

The specific decision criteria used to define "limited evidence for carcinogenicity" should be clarified. If the criteria of another organization are being used, they should be cited.

State of California

M E M O R A N D U M

To : Kimi Klein
Dept. of Food and Agriculture
1220 N Street
Sacramento, CA 95814

Date : December 30, 1987

Subject : Comments on Draft Ethyl Parathion Report

Robert Barham, Chief
Toxic Air Contaminant
Identification Branch

From : **Air Resources Board**

We have reviewed the December 1987 draft report Evaluation of Ethyl Parathion As A Toxic Air Contaminant and offer the following comments:

1. Tables 3 and 4 indicate that more ethyl parathion was used in Sutter County during May and throughout 1985 than was used in Imperial County in the autumn or throughout 1985. Page 8 appears to be incorrect in stating that the two areas of most frequent applications are the San Joaquin Valley and Imperial County. We suggest that the draft report identify reasons for not recommending monitoring for ethyl parathion in Sutter County during May.

2. On pages 23, 29, and 38, the minimum detection limit (MDL) for paraoxon is incorrectly stated as 0.01 ug/m^3 or 0.9 ppt. This MDL is correctly presented in Table 8B as 0.02 ug/m^3 or 1.6 ppt.

3. On page 24, the CDFA monitoring recommendation is stated to have been for Kings County. This should be Kern County.

4. In Tables 6 and 7, it is not clear why overall means were not calculated for the background sites.

5. In Tables 8A-8D and 9, the meaning of the symbol "-" is unclear. For days for which there were no data available, a reason should be given such as "not determined." Otherwise, it appears that no sample was collected.

6. In Table 8D, footnote b is unneeded because no paraoxon was detected in the samples summarized in that table.

7. On page 36, the report correctly states that no short-term data are available from the ARB monitoring. Because of this, on page 39 the maximum 24-hour concentration was used to estimate risk from acute exposure. We do not recommend using 24-hour concentrations to be representative of maximum short-term exposure. To estimate risk from acute exposure, we recommend

that the draft report cite short-term parathion concentrations measured by CDFA. One study (A Study of Downwind Drift of Parathion from Applications in the Antelope Valley of Los Angeles County, CA in April 1982, K. Maddy et al., HS-1087, August 1983) conducted adjacent to a parathion application reported a maximum 20 minute concentration of 33.9 ug/m^3 which is one third of the 8-hour TLV.

If you have questions regarding our comments, please call Lynn Baker at 3-8511.

cc: Dave Duncan
Bill Lockett
Ron Oshima

VIII. Correspondence with the Scientific Review Panel

UNIVERSITY OF CALIFORNIA

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO

SANTA BARBARA • SANTA CRUZ

[illegible]

[illegible]

403 Giannini Hall
College of Natural Resources
Berkeley, California 94720

February 4, 1988

Mr. Jack Parnell, Director
California Department of
Food and Agriculture
1220 N Street
Sacramento, CA 95814

Dear Mr. Parnell:

The purpose of this letter is to advise you of the actions taken by the Scientific Review Panel (SRP) at its January 25 meeting on the California Department of Food and Agriculture (CDFA) report for Ethyl Parathion. There are a number of points in the report needing clarification so as to make the report scientifically and technically adequate.

The Panel is requesting five specific items:

1- More population exposure data.
2- Change or remove the statement recommending the Panel declare Ethyl Parathion not to be a Toxic Air Contaminant.
3- Supply more risk assessment studies of the cholinesterase levels in high risk groups such as one to six month old infants.
4- The cumulative effect of cholinesterase inhibitors should be considered.
5- Provide a description of the pesticide enforcement laws which pertain to human health with an explanation of the parameters of each law as determined and enforced by the CDFA.

We are pleased with the presentation made by your staff, particularly Ms. Kathy Brunetti. We appreciate the department's commitment to making the changes above in time for Panel review prior to our February 29 meeting in San Francisco.

I would like to suggest that it may be helpful to coordinate the legal analysis with Jananne Sharpless' Office.

If you have any questions or concerns, please contact me at (415) 526 - 1031.

Sincerely,

Dr. James B. Kendrick
Chairman
Scientific Review Panel

cc: Panel Members
Jananne Sharpless
Ms. Kathy Brunetti

DEPARTMENT OF FOOD AND AGRICULTURE
1220 N Street, P. O. Box 942871
Sacramento, California 94271-0001

February 19, 1988

Dr. James B. Kendrick, Chairperson
Scientific Review Panel
615 Spruce Street
Berkeley, CA 94707

Dear Dr. Kendrick:

Final Draft of Ethyl Parathion as a Toxic Air Contaminant
February 1988

Enclosed for your review is a final draft of "Evaluation of Ethyl Parathion as a Toxic Air Contaminant - February 1988." In response to the requests of the Panel as outlined in your letter dated 4 February 1988 to the Director, the following revisions have been made:

1) Table 10, showing the population of the monitoring sites, has been added, along with a brief discussion concerning the relationship between those populations and measured ambient air levels (pages 43-44);

2) The recommendation in the Executive Summary as well as the recommendation section has been removed;

3) A statement has been added in the conclusion of the risk assessment section that a 20-fold margin of safety was necessary for infants and children based on lower cholinesterase values in infants and lower LD_{50}'s in newborn rats compared to adult rats (pages 103, 105); and

4) The potential for concurrent exposures to other cholinesterase inhibitors has been acknowledged, although such exposures were not factored into the document (pages 17, 106).

Further revisions in response to comments from the SRP at the meeting of 25 January 1988 are as follows:

- Table 5, depicting reported ambient air levels, has been revised and expanded. A discussion of those studies has been included (pages 14-17);

- The section on conversion of parathion to paraoxon has been expanded to more concisely describe the conditions promoting phototransformation (pages 11-12);

- The mutagenicity section has been expanded to include tables of all studies. The conclusions from this section has been reworded with greater weight placed on the positive results so that overall conclusions were more equivocal to positive rather than negative to equivocal (pages 86-94);

- The oncogenicity section has been revised with the addition of Table 17 and an expanded description of oncogenicity studies (pages 95-97); and

- The criteria for determination of carcinogenicity in the risk assessment section has been expanded (pages 102-103).

If you or any other panel members have any questions, please contact Kathy Brunetti at (916) 324-8916.

Sincerely,

A. Kimiko Klein

A. Kimiko Klein, Ph.D.
Associate Environmental Hazards Scientist
Environmental Hazards Assessment Program
Environmental Monitoring and
Pest Management, Room A-149
(916) 445-5003

Enclosure

cc: Scientific Review Panel Members
William Lockett
Rex Magee
Robert Peterson
Kathy Brunetti
David Duncan
Deborah Oudiz
Keith Pfieffer
Larry Nelson

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and Natural Resources, Emeritus

303 Giannini Hall
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Berkeley, California 94720

April 26, 1988

Mr. Jack Parnell, Director
California Department of
Food and Agriculture
1220 N Street
Sacramento, CA 95814

Dear Mr. Parnell:

At the March 28, 1988 Scientific Review Panel meeting we found the revised CDFA report "Evaluation of Ethyl Parathion As A Toxic Air Contaminant", to be seriously deficient. To overcome these deficiencies, the SRP recommends the following:

- Include in the report a complete literature search of ethyl parathion and paraoxon pesticide exposure concentrations, providing information not contained in the initial literature search.

- In coordination with ARB staff, include in the report a complete presentation of all ARB and CDFA information on air concentrations of ethyl parathion and paraoxon. The presentation should include tables and a discussion of air concentration data generated during and subsequent to application. This data should include on-site exposure concentrations, adjacent field exposure concentrations (such as the Maddy (1983) data), and offsite, down wind, ambient exposure concentrations.

- Include a detailed presentation of pesticides in fog, and an analysis of their potential to result in exposure to human populations.

- In coordination with ARB staff, describe currently available exposure profile modeling performed by CDFA, ARB, and in the literature.

- Include a table of Margin of Safety at selected concentration levels, for the conditions of acute, sub-acute, and chronic exposures, with particular reference to the most sensitive sub-population (i.e. infants).

By following these recommendations, the CDFA report will be ready for re-evaluation of its scientific merit. If you have any further questions, please call me at ATSS 8-477-7171.

Sincerely,

Dr. James Kendrick
Chairman
Scientific Review Panel

cc Panel Members
Jananne Sharpless
Dr. Ron Oshima
William Lockett

STATE OF CALIFORNIA

GEORGE DEUKMEJIAN, Governor

DEPARTMENT OF FOOD AND AGRICULTURE

1220 N Street, P.O. Box 942871
Sacramento, California 94271-0001

May 11, 1988

Dr. James Kendrick
Chairman
Scientific Review Panel
615 Spruce Street
Berkeley, California 94707

Dear Dr. Kendrick:

At the March 28, 1988 meeting, the Scientific Review Panel found the revised CDFA report, "Evaluation of Ethyl Parathion As a Toxic Air Contaminant", to be seriously deficient. Your recent letter made specific recommendations to overcome these deficiencies. All of these recommendations have been addressed. Revised portions of the report will be sent to all panel members for their review prior to the meeting scheduled for May 25, 1988. A summary of the revisions is outlined below.

1. Another literature search was performed, and, as a result, ten pertinent citations were added to the bibliography. Of these, the results of two studies of occupational exposures were added to the report, and make up the data appearing in Table 5A. Additionally, the results of an unpublished study performed by the CDFA appear in revised Table 5D.

2. Revised Table 5A-D presents the information requested on occupational exposure and on-site, adjacent, off-site, and ambient airborne levels of parathion. Included with these data are two studies by Maddy et al. (1982, 1983).

3. A section on ambient airborne levels in fog has been added as requested (II. Background, D. Airborne levels reported in the literature, 4. Ambient airborne levels in fog).

4. A discussion of the air dispersion model used by the ARB to determine the location of sampling sites has been included (II. Background, E. Use of Models to estimate air levels of ethyl parathion). To date, the CDFA has not carried out any air modeling of any pesticide, because there are no models currently available that are scientifically appropriate and validated for such use. The CDFA staff has not found any air modeling studies of ethyl parathion in the open literature.

5. A table of margin of safety values at specific concentrations for acute, subchronic and chronic exposures has been included as requested.

6. In addition to the revisions made in response to the recommendations of the Scientific Review Panel, a discussion of the decision of the U.S. EPA to place ethyl parathion in special review has been added (II. Background, A. Toxicity and Regulation of Ethyl Parathion).

On behalf of the staff at the CDFA, I would like to thank the members of the panel for their thoughtful and constructive comments both in regard to this report and in regard to the AB1807/3219 process.

Sincerely,

COPY: Original Signed By Jack C. Parnell

Jack C. Parnell
Director
(916) 445-7126

cc: Panel Members
Jananne Sharpless
Ronald Oshima
William Lockett

STATE OF CALIFORNIA GEORGE DEUKMEJIAN, Governor

DEPARTMENT OF FOOD AND AGRICULTURE
1220 N Street, P.O. Box 942871
Sacramento, California 94271-0001

May 20, 1988

Dr. James B. Kendrick
Chairperson
Scientific Review Panel
615 Spruce Street
Berkeley, CA 94707

Dear Dr. Kendrick:

Revised Final Draft of Ethyl Parathion as a
Toxic Air Contaminant, May 1988

Enclosed is the revised final draft of the report "Evaluation of Ethyl Parathion as a Toxic Air Contaminant", dated May 1988. In response to the recommendations made by the Panel, detailed in your letter of April 26, 1988 to the Director, the revisions outlined in Items 1 through 6 have been made:

1. Another literature search was performed, and, as a result, ten pertinent citations were added to the bibliography. Of these, the results of two studies of occupational exposures were added to the report and make up the data appearing in Table 5A (pg.17). Additionally, the results of an unpublished study performed by the CDFA appear in revised Table 5D (pg.23).

2. Revised Tables 5A-D present the information requested on occupational exposure and on-site, adjacent, off-site, and ambient airborne levels of parathion (pg. 15 to 24). Included with these data are two studies by Maddy et al. (1982, 1983). This revised section was reviewed and approved by the ARB staff.

3. A section on ambient airborne levels in fog has been added as requested (pg. 25).

4. A discussion of the air dispersion model used by the ARB to determine the location of sampling sites has been included (pg. 26). This section was reviewed by the ARB staff, and their comments were incorporated into the discussion. Brief mention is made of other models which may be used for pesticide dispersion in air, and three citations referring to air dispersion modeling have been added to the bibliography. To date, the CDFA has not carried out any air modeling of any pesticide, because none of the models currently available has been proven to be scientifically appropriate or has been validated for such use. Furthermore, the input data for such models are quite poor or nonexistent. The CDFA staff has not found any air modeling studies of ethyl parathion in the open literature.

5. A table was added to the risk assessment section which estimated exposure values for 10-fold and 100-fold margins of safety (Table 19, pg. 124).

Subsequent to suggestions made by Dr. Pitts on 12 May 1988, the following revisions have also been made:

6. The last statement in the introduction has been rearranged for greater clarity (pg. 2).

7. The structural formula for ethyl parathion in Figure 1 has been corrected (pg 4).

8. The term active ingredient has been defined (pg. 11).

9. The conversion to paraoxon section has been expanded to include a discussion of the lifetime of parathion and paraoxon in the presence of atmospheric oxidants, and a brief mention of the hydrolysis half-life of parathion has been added (pg. 12-13).

10. The comments in Table 5A have been clarified (pg 17).

11. The data reported by Carman et al (1952) have been eliminated from Table 5D and are discussed in the text only (pg. 23 and pg 24).

12. A discussion of the possible mechanisms of conversion of parathion to paraoxon in fog has been included (pg. 26)

13. The range of values found in the rural communities of the central valley has been included in the discussion on modeling (pg.27).

14. The sensitivity of the method of analysis used by the ARB relative to its ability to detect ethyl parathion near a site of application has been addressed (pg. 56).

In addition to the revisions made in response to the recommendations of the Scientific Review Panel, several other revisions have been made:

15. A discussion of the decision of the U.S. EPA to place ethyl parathion in special review has been added (pg. 6).

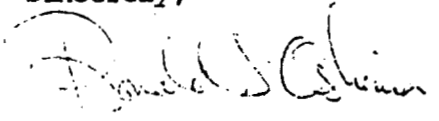
16. Measured paraoxon values were converted to parathion equivalent values, weighted by a factor of ten for increased toxicity and added to measured parathion values (Table 8C, pg. 48). Risk estimates were recalculated with these adjusted data (Table 18, pg.123).

17. Health effects data (acute lethal doses) were added to Table 11, pg. 87.

18. Risks for acute exposures from offsite drift were calculated (Table 18, pg. 123).

If you or other panel members have any questions regarding these revisions, please contact Kathy Brunetti at (916) 324-8916.

Sincerely,



Ronald Oshima
Branch Chief
Environmental Monitoring and
Pest Management, Room A-149
(916) 324-8916

Enclosure

cc: Scientific Review Panel Members
Rex Magee
William Lockett
Bruce Oulrey
Kathy Brunetti
David Duncan
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303 Giannini Hall
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Berkeley, California 94720

June 20, 1988

Mr. Jack Parnell, Director
California Department of
Food and Agriculture
1220 N Street
Sacramento, CA 95814

Dear Mr. Parnell,

At our May 25, 1988 Scientific Review Panel meeting, the Panel found CDFA's report "Evaluation of Ethyl Parathion as a Toxic Air Contaminant" to be without serious deficiency. At this meeting the Panel also recommended that CDFA identify Ethyl Parathion as a toxic air contaminant.

I sincerely appreciate the successful effort CDFA has made in aiding the SRP in the report evaluation. I see our work together to date as streamlining the process on future reports.

Enclosed is a copy of the Scientific Review Panel's Findings on Ethyl Parathion.

Sincerely,

Dr. James B. Kendrick,
Chairman
Scientific Review Panel

cc: Panel Members

Report of the Scientific Review Panel on
EVALUATION OF ETHYL PARATHION AS A TOXIC AIR CONTAMINANT
as adopted on May 25, 1988

In accordance with the provisions of Health and Safety Code Section 39661, the Scientific Review Panel (SRP) has reviewed the report of the staff of the California Department of Food and Agriculture on the public exposure and biologic and health effects of ethyl parathion, and the public comments on this report. Based on this review, the SRP finds that the report is without serious deficiency and further finds that:

1. Ethyl parathion and its oxidized product paraoxon are potent neurotoxins.

2. There is only limited evidence for the carcinogenicity of parathion in animals and there are inadequate data to evaluate the carcinogenic potential of parathion for humans.

3. Because of its high toxicity, ethyl parathion can only be used as a pesticide under permit; regulations govern use conditions and worker reentry standards.

4. The report contains analyses of margin of safety (MOS) for acute, subchronic and chronic effects of ethyl parathion, using cholinesterase inhibition as the most sensitive index of effect. The CDFA concluded that adverse health effects from exposure to ethyl parathion would be unlikely with levels attained at sites remote from those of pesticide application. The smallest calculated MOS using available off-site exposure data is 12. This is the figure derived for children, who are more sensitive than adults, and assumes exposure of several weeks to ambient concentrations of 0.17 ug/m3. A margin of safety of 12 is small. In addition, the margin of safety may be reduced in especially susceptible populations (asthmatics, patients on B-adrenergic blockade therapy or acetylcholinesterase inhibition therapy, and neonates) and by the presence

of other cholinesterase inhibitors in the air. The calculated MOS for acute off-site exposure is 74 for children. This is higher than for subchronic exposure, but is less reliable because the calculation is based on the highest off-site concentration reported in the literature (34ug/m3). In fact, accidental exposures to concentrations considerably higher than 34ug/m3 are possible at and immediately adjacent to application sites. This is borne out by occasional reports of poisoning.

For these reasons we recommend that ethyl parathion be listed as a toxic air contaminant.

I certify that the above is a true and correct copy of the findings adopted by the Scientific Review Panel on May 25, 1988.

Dr. James B. Kendrick, Chairman
Scientific Review Panel